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SESSION RESUMED IN FILE 'REGISTRY' AT 20:47:15 ON 23 SEP 2004
FILE 'REGISTRY' ENTERED AT 20:47:15 ON 23 SEP 2004
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.10       2.31

=> d his

     (FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1              STRUCTURE UPLOADED
L2           50 S SAM L1

=> s l1 full
FULL SEARCH INITIATED 20:47:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 491947 TO ITERATE

 81.3% PROCESSED  400000 ITERATIONS                          62637 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       491947 TO   491947
PROJECTED ANSWERS:           76203 TO    77867

L3        62637 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   157.52     157.73

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
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FILE COVERS 1907 - 23 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004 (20040922/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3 and receptor
23107 L3
571186 RECEPTOR
L4 771 L3 AND RECEPTOR

=> s l4 and ligand
264845 LIGAND
L5 73 L4 AND LIGAND

=> t ti l5 1-50

L5 ANSWER 1 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate **receptor** antagonists

L5 ANSWER 2 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI [3H]A-317491, a novel high-affinity non-nucleotide antagonist that specifically labels human P2X2/3 and P2X3 receptors

L5 ANSWER 3 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Dye-Labeled Benzodiazepines: Development of Small Ligands for **Receptor** Binding Studies Using Fluorescence Correlation Spectroscopy

L5 ANSWER 4 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Fluorescent ligands and measuring of binding of samples to androgen **receptor**

L5 ANSWER 5 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 4-(phenylpiperazinylmethyl)benzamides for treatment of pain or gastrointestinal disorders

L5 ANSWER 6 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Ligands for the peroxisome proliferator-activated **receptor**

L5 ANSWER 7 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of a novel diphosphine-palladium macrocyclic complex possessing a molecular recognition site. Oxidative addition studies

L5 ANSWER 8 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Design and Synthesis of Novel Dimeric Morphinan Ligands for κ and μ Opioid Receptors

L5 ANSWER 9 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Rational Design and Synthesis of Androgen **Receptor**-Targeted Nonsteroidal Anti-Androgen Ligands for the Tumor-Specific Delivery of a Doxorubicin-Formaldehyde Conjugate

L5 ANSWER 10 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI 2', 3'-O-(2,4,6, trinitrophenyl)-ATP and A-317491 are competitive antagonists at a slowly desensitizing chimeric human P2X3 **receptor**

L5 ANSWER 11 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of pyridones as modulators of nuclear receptors, including liver X **receptor** (LXR).

L5 ANSWER 12 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Novel fluorescence based **receptor** binding assay method for receptors lacking **ligand** conjugates with preserved affinity: Study on estrogen **receptor** α

L5 ANSWER 13 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of novel bivalent multi-binding phenolic amino compounds as β2-adrenergic **receptor** agonists

L5 ANSWER 14 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI A novel strapped porphyrin **receptor** for molecular recognition

L5 ANSWER 15 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthetic Inhibitors of Proline-Rich **Ligand**-Mediated Protein-Protein Interaction: Potent Analogs of UCS15A

L5 ANSWER 16 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of piperidino cannabinoid **receptor** ligands

L5 ANSWER 17 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of benzotriazepines as gastrin and cholecystokinin **receptor** ligands for treating gastrointestinal disorders

L5 ANSWER 18 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI cDNAs encoding human olfactory cyclic nucleotide gated (CNG) channel subunits for use in enhancing smell receptors

L5 ANSWER 19 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of [1,2']bipyrazinyl 5-HT2 **receptor** ligands for treatment of sexual dysfunction

L5 ANSWER 20 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Exponential pattern recognition-based cellular targeting, compositions, methods and anticancer applications

L5 ANSWER 21 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

L5 ANSWER 22 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

L5 ANSWER 23 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and Investigation of New Macrocyclic Diphosphine-Palladium(0) Complexes Based on the Barbiturate Binding **Receptor**

L5 ANSWER 24 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Anion-Templated Rotaxane Formation

L5 ANSWER 25 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Refinement and evaluation of a pharmacophore model for flavone derivatives binding to the benzodiazepine site of the GABAA **receptor**

L5 ANSWER 26 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of nicotinanilide-N-oxides as G-protein-coupled **receptor** antagonist for the treatment of inflammation due to

neutrophil chemotaxis

L5 ANSWER 27 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Environment and mobility of a series of fluorescent reporters at the amino terminus of structurally related peptide agonists and antagonists bound to the cholecystokinin **receptor**

L5 ANSWER 28 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of naphthalene derivatives as cannabinoid CB1 **receptor** ligands.

L5 ANSWER 29 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of novel multi-binding phenolic compounds as β2-adrenergic **receptor** agonists

L5 ANSWER 30 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Comparative binding energy (COMBINE) analysis of human neutrophil elastase inhibition by pyridone-containing trifluoromethylketones

L5 ANSWER 31 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Pharmacological analysis of CCK2 **receptor** ligands using COS-7 and SK-N-MC cells, expressing the human CCK2 **receptor**

L5 ANSWER 32 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of imidazoles as gastrin and cholecystokinin **receptor** ligands for treatment of gastrointestinal disorders

L5 ANSWER 33 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and pharmaceutical compositions of gastrin/cholecystokinin **receptor** ligands with proton pump inhibitors

L5 ANSWER 34 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Analysis of fluorescently labeled substance P analogs: binding, imaging and **receptor** activation

L5 ANSWER 35 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Validation of flow cytometric competitive binding protocols and characterization of fluorescently labeled ligands

L5 ANSWER 36 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Therapeutic uses of PPAR mediators as ABC-1 expression modulators, and preparation thereof

L5 ANSWER 37 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI NF449: a subnanomolar potency antagonist at recombinant rat P2X1 receptors

L5 ANSWER 38 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and characterization of new aromatic tweezers and complex formation with tropylium ion in 1,2-dichloroethane

L5 ANSWER 39 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 4-(arylhydroxyethylaminoethyl)phenylaminohydroxyethylbenzenes and related compounds as β2 adrenergic **receptor** agonists and partial agonists.

L5 ANSWER 40 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Nonpeptide cholecystokinin-2 **receptor** agonists

L5 ANSWER 41 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of novel multibinding phenolic compounds as β2-adrenergic **receptor** agonists

L5 ANSWER 42 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of inositol 1,4,5-triphosphate derivatives as IP3 **receptor** ligands

L5 ANSWER 43 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Use of triazolopyridazine GABAA **receptor** ligands for treating premenstrual syndrome

L5 ANSWER 44 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Tri-aryl acid derivatives as PPAR **receptor** ligands

L5 ANSWER 45 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation gastrin and cholecystokinin **receptor** ligands

L5 ANSWER 46 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Estimation of **Receptor-Ligand** Interactions by the Use of a Two-Marker System in Affinity Capillary Electrophoresis

L5 ANSWER 47 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Chiral, metal templated self-assembly

L5 ANSWER 48 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of multibinding piperidinylindole derivatives as therapeutic agents that modulate 5-HT receptors

L5 ANSWER 49 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Dual avb3 and metastasis-associated **receptor** ligands

L5 ANSWER 50 OF 73 CAPLUS COPYRIGHT 2004 ACS on STN
TI Chemical probes that differentially modulate peroxisome proliferator-activated **receptor** α and BLTR, nuclear and cell surface receptors for leukotriene B4

=> d scan l5

L5 73 ANSWERS CAPLUS COPYRIGHT 2004 ACS on STN
CC 1-6 (Pharmacology)
Section cross-reference(s): 21
TI Rational Design and Synthesis of Androgen **Receptor**-Targeted Nonsteroidal Anti-Androgen Ligands for the Tumor-Specific Delivery of a Doxorubicin-Formaldehyde Conjugate
ST androgen **receptor** prostate tumor nonsteroidal antiandrogen doxorubicin formaldehyde conjugate
IT Androgens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogens; rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)
IT Antitumor agents
Drug delivery systems
Drug design
Human
Prostate gland, neoplasm
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)
IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a

doxorubicin-formaldehyde conjugate)

IT 636595-46-5P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT **636595-77-2P 636595-79-4P 636595-81-8P**
636595-90-9P 636595-92-1P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT **636595-44-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT 65-45-2, Salicylamide 13311-84-7, Flutamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT **636595-94-3**
RL: PRP (Properties)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT 76143-20-9P **636595-48-7P** 636595-54-5P 636595-56-7P
636595-58-9P 636595-61-4P 636595-63-6P 636595-66-9P 636595-74-9P
636595-83-0P 636595-85-2P 636595-86-3P 636595-88-5P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT **636595-41-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT 77-71-4 36894-69-6, Labetalol 194853-86-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

IT **636595-50-1P 636595-52-3P** 636595-68-1P 636595-71-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(rational design and synthesis of androgen **receptor**-targeted nonsteroidal anti-androgen ligands for tumor-specific delivery of a doxorubicin-formaldehyde conjugate)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his

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     (FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1             STRUCTURE UPLOADED
L2              50 S SAM L1
L3           62637 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4             771 S L3 AND RECEPTOR
L5              73 S L4 AND LIGAND

=> s l5 and (divalent or multivalent or dimeric or multimeric or multipartite or
dipartite)
          63043 DIVALENT
           9338 MULTIVALENT
          34512 DIMERIC
           3637 MULTIMERIC
            230 MULTIPARTITE
              2 DIPARTITE
L6            5 L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR
                MULTIPARTITE OR DIPARTITE)

=> t ti l6 1-5

L6   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Design and Synthesis of Novel Dimeric Morphinan Ligands for
     κ and μ Opioid Receptors

L6   ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of novel bivalent multi-binding phenolic amino compounds as
     β2-adrenergic  receptor agonists

L6   ANSWER 3 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of novel multi-binding phenolic compounds as
     β2-adrenergic  receptor agonists

L6   ANSWER 4 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of novel multibinding phenolic compounds as β2-adrenergic
     receptor agonists

L6   ANSWER 5 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of multibinding piperidinylindole derivatives as therapeutic
     agents that modulate 5-HT receptors


=> d ibib abs l6 1-5

L6   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2003:840480  CAPLUS
DOCUMENT NUMBER:         140:42322
TITLE:                   Design and Synthesis of Novel Dimeric
                         Morphinan Ligands for κ and μ Opioid
                         Receptors
AUTHOR(S):               Neumeyer, John L.; Zhang, Ao; Xiong, Wennan; Gu,
                         Xiao-Hui; Hilbert, James E.; Knapp, Brian I.; Negus,
                         S. Stevens; Mello, Nancy K.; Bidlack, Jean M.
CORPORATE SOURCE:        Alcohol and Drug Abuse Research Center, Harvard
                         Medical School, McLean Hospital, Belmont, MA, 02478,
                         USA
SOURCE:                  Journal of Medicinal Chemistry (2003), 46(24),
                         5162-5170
```

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:42322
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

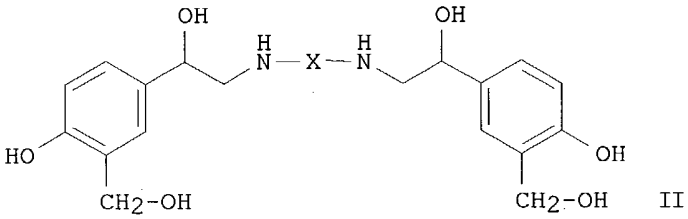
AB A novel series of morphinans were synthesized, and their binding affinity at and functional selectivity for μ, δ, and κ opioid receptors were evaluated. These **dimeric** ligands can be viewed as **dimeric** morphinans, which were formed by coupling two identical morphinan pharmacophores (cyclorphan or MCL 101) with varying connecting spacers. Ligands with alkyl spacers on the nitrogen position and ligands in which the two morphinan pharmacophores were coupled by ether moieties at the 3-hydroxyl positions showed significant decrease in affinity at all three opioid receptors. An improvement in the affinity was achieved by introducing an ester moiety as the spacer in the **dimeric** morphinans. It was observed that the affinity of these ligands was sensitive to the character and length of the spacer. I (X = (CH2)2) (MCL-139) with a 4-carbon ester spacer, I (X = (CH2)8) (MCL-144) containing a 10-carbon spacer, and (X = CH:CH) with the conformationally constrained fumaryl spacer were the most potent ligands in this series, displaying excellent affinities at μ and κ receptors (Ki = 0.09-0.2 nM at μ and Ki = 0.078-0.049 nM at κ), which were comparable to the parent compound II , a compound containing only one morphinan pharmacophore and a long-chain ester group, had affinity at both μ and κ receptors almost identical to that of the parent **ligand.** In the [35S]GTPγS binding assay, ligands I (X = (CH2)2, (CH2)8, CH:CH) and their parent morphinans stimulated [35S]GTPγS binding mediated by the μ and κ receptors. I (X = (CH2)2, (CH2)8) were full κ agonists and partial μ agonists, while I (X = CH:CH) was a partial agonist at both μ and κ receptors. These novel ligands, as well as their interesting pharmacol. properties, will serve as the basis for our continuing investigation of the **dimeric** ligands as potential probes for the pharmacotherapy of cocaine abuse and may also open new avenues for the characterization of opioid receptors.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:545792 CAPLUS
DOCUMENT NUMBER: 139:100926
TITLE: Preparation of novel bivalent multi-binding phenolic amino compounds as β2-adrenergic **receptor** agonists
INVENTOR(S): Choi, Seok-Ki; Moran, Edmund J.
PATENT ASSIGNEE(S): Theravance, Inc., USA
SOURCE: U.S., 63 pp., Cont. of U.S. Ser. No. 323,939, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6593497	B1	20030715	US 2000-504761	20000214
PRIORITY APPLN. INFO.:			US 1999-323939	B1 19990602
OTHER SOURCE(S):	MARPAT 139:100926			

GI



II

AB Novel bivalent, multi-binding, phenolic amine compds. LpXq (I) are disclosed [wherein: L = β-hydroxy-β-arylethylamine-based **ligand**, linked at carbon or nitrogen; X = specified, optionally repeating linker; p = 2-10; q = 1-20]. Compds. I are β2-adrenergic **receptor** agonists (no data), and are therefore useful in the treatment and prevention of respiratory diseases such as asthma, bronchitis, and the like. I are also useful in the treatment of nervous system injury and premature labor. Claims cover, in particular, compds. Ar1-CH(OH)CH2-NH-X-NH-CH2CH(OH)-Ar2 [where: Ar1, Ar2 = certain (un)substituted Ph groups; X = (CH2)6-O-[(CH2)6-O]0-9(CH2)6]. Ten compound synthetic examples are given for II [X = various monomeric, polymeric, and oligomeric (poly)oxyalkylene chains]. Compds. II were prepared from 5-acetylsalicylic acid Me ester via: (1) oxidation to α,α-dihydroxy-4-hydroxy-3-(methoxycarbonyl)acetophenone using HBr in DMSO, and (2) condensation of the latter with various diamines and borane reduction of the formed intermediate imines. In addition, combinatorial arrays of **multimeric** ligands and methods of assaying the **multimeric ligand** libraries for β2-adrenergic agonist activity are embodied by the invention. Formulations for capsules, tablets, a dry powder inhaler, suppositories, suspensions, and topical forms are described.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:354101 CAPLUS
DOCUMENT NUMBER:	136:355062
TITLE:	Preparation of novel multi-binding phenolic compounds as β2-adrenergic **receptor** agonists
INVENTOR(S):	Moran, Edmund J.; Griffin, John H.; Choi, Seok-ki
PATENT ASSIGNEE(S):	Theravance, Inc., USA
SOURCE:	U.S. Pat. Appl. Publ., 92 pp., Cont. of U.S. Ser. No. 323,943. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	31

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002055651	A1	20020509	US 2001-934982	20010821

US 6683115	B2	20040127			
US 6541669	B1	20030401	US 1999-323943		19990602
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AU 9945435	A1	19991230	AU 1999-45435		19990604
EP 1003540	A1	20000531	EP 1999-928344		19990604
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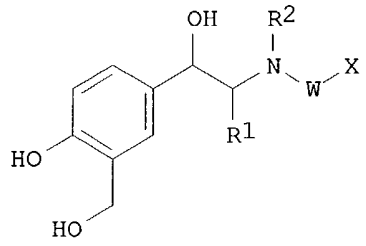

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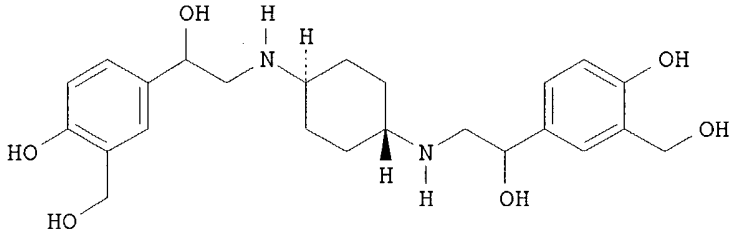

II

AB Methods for preparing novel multibinding phenolic compds., LpXq [where L = a **ligand** capable of binding to a β2-adrenergic **receptor** ; X = a linker; p = 2-10; q = 1-20], which serve as β2-adrenergic **receptor** agonists, are disclosed. Preferred ligands are of formula I [R1 = H, (un)substituted alkyl, or a bond linking **ligand** to linker; R2 = H, aralkyl, acyl, (un)substituted alkyl, cycloalkyl or a bond linking **ligand** to linker; W = bond, (un)substituted alkylene wherein one or more carbon atoms is optionally replaced by NR3, O, S, SO, SO2, CO, P-alkyl, PO2, OP(O)O or the alkylene optionally links the **ligand** to a linker with provisions; R3 = H, alkyl, acyl, or bond linking **ligand** to linker; X = aryl, heteroaryl, heterocyclyl and (un)substituted cycloalkyl wherein each X optionally links the **ligand** to the linker]. II was prepared from α,α-dihydroxy-4-hydroxy-3-methoxycarbonylacetophenone via condensation with trans-1,4-diaminocyclohexane with subsequent reduction of intermediate imine. In addition, combinatorial arrays of **multimeric** ligands and methods of assaying the **multimeric** ligands are embodied by the invention. As β2-adrenergic **receptor** agonists, the compds. are useful in the treatment and prevention of respiratory diseases such as asthma, bronchitis (no data). The title compds. are also useful in the treatment of nervous system injuries and premature labor. Formulations for capsules, tablets, dry power inhaler, suppositories and suspensions are described.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:102476 CAPLUS
DOCUMENT NUMBER: 134:131310
TITLE: Preparation of novel multibinding phenolic compounds as β2-adrenergic **receptor** agonists

INVENTOR(S): Griffin, John H.; Moran, Edmund J.; Choi, Seok-Ki
PATENT ASSIGNEE(S): Advanced Medicine, Inc., USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 31
PATENT INFORMATION:

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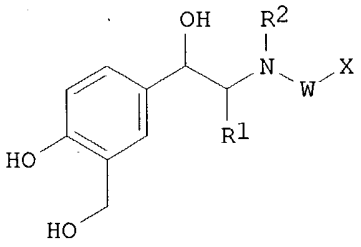

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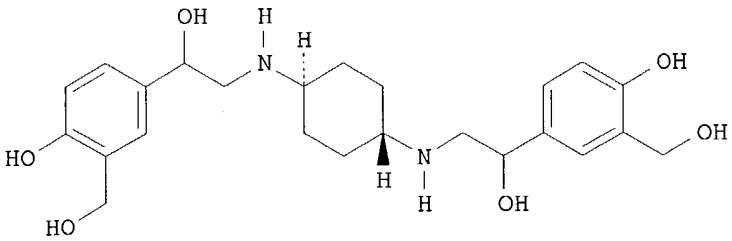

II

AB Methods for preparing novel multibinding phenolic compds., LpXq [where L = a **ligand** capable of binding to a β2-adrenergic **receptor** ; X = a linker; p = 2-10; q = 1-20], which serve as β2-adrenergic **receptor** agonists, are disclosed. Preferred ligands are of formula I [R1 = H, (un)substituted alkyl, or a bond linking **ligand** to linker; R2 = H, aralkyl, acyl, (un)substituted alkyl, cycloalkyl or a bond linking **ligand** to linker; W = bond, (un)substituted alkylene wherein one or more carbon atoms is optionally replaced by NR3, O, S, SO, SO2, CO, P-alkyl, PO2, OP(O)O or the alkylene optionally links the **ligand** to a linker with provisions; R3 = H, alkyl, acyl, or bond linking **ligand** to linker; X = aryl, heteroaryl, heterocyclyl and (un)substituted cycloalkyl wherein each X optionally links the **ligand** to the linker]. II was prepared from α,α-dihydroxy-4-hydroxy-3-methoxycarbonylacetophenone via condensation with trans-1,4-diaminocyclohexane with subsequent reduction of intermediate imine. In addition, combinatorial arrays of **multimeric** ligands and methods of assaying the **multimeric** ligands are embodied by the invention. As β2-adrenergic **receptor** agonists, the compds. are useful in the treatment and prevention of respiratory diseases such as asthma, bronchitis (no data). The title compds. are also useful in the treatment of nervous system injuries and premature labor. Formulations for capsules, tablets, dry power inhaler, suppositories and suspensions are described.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:795681 CAPLUS
DOCUMENT NUMBER: 132:35606
TITLE: Preparation of multibinding piperidinylindole derivatives as therapeutic agents that modulate 5-HT receptors
INVENTOR(S): Marquess, Daniel; Griffin, John H.; Choi, Seok-Ki
PATENT ASSIGNEE(S): Advanced Medicine, Inc., USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 31
PATENT INFORMATION:

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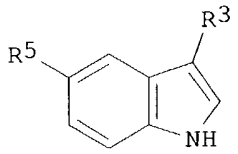

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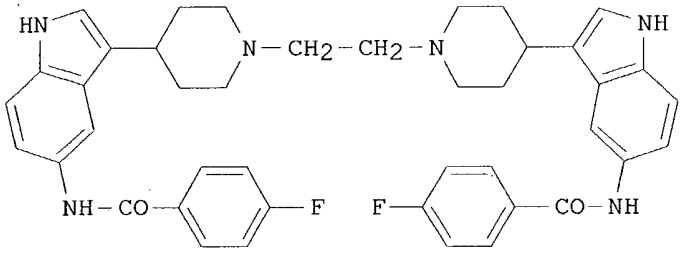

II

AB Novel multibinding piperidinylindole compds, LpXq [where L = a **ligand** capable of binding to a 5-HT **receptor**; X = a linker; p = 2-10; q = 1-2], that modulate 5-HT receptors are disclosed. Preferred ligands are of formula I [where R3 and R5 = independently point of attachment of the linker, H, alkyl, heterocyclic, heteroaryl(alkyl), amidoalkyl, (di)alkylaminosulfonylalkyl, arylsulfonylalkyl, heterocyclosulfonylalkyl, arylcarbonylamino, alkylsulfonamido, or alkylsufonylalkyl]. Over 140 multibinding compds., formed from two piperidinylindole derivs. and a difunctional linker, were prepared For example, condensation of 5-(4-fluorobenzoyl)amino-3-(piperidin-4-yl)-1H-indole with 1,2-dibromoethane at 72° in DMF, after workup and chromatog., yielded the dimer II. Compds. of this invention are useful in the treatment of migraine, headache, itch, motion sickness, depression, emesis, memory loss, anxiolytic disorders, obesity, gastrointestinal disorders, and irritable bowel syndrome (no data). The multibinding compds. provide greater biol. and/or therapeutic effects than the aggregate of the unlinked ligands due to their multibinding properties (no data). Combinatorial arrays, methods of synthesis, and methods of assaying the **dimeric** and **multimeric** compds. are also embodied by the invention.

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IC    ICM  G01N033-58
      ICS  G01N033-68; G01N033-533
CC    9-11 (Biochemical Methods)
      Section cross-reference(s): 1, 3, 13
TI    Methods for detecting modulators of ion channels using thallium (i)
      sensitive assays
ST    thallium cell culture media ion channel receptor drug screening
IT    Receptors
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (5-hydroxytryptamine-gated; methods for detecting modulators of ion
         channels using thallium (i) sensitive assays)
IT    Glutamate receptors
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazoleproprionate);
         methods for detecting modulators of ion channels using thallium (i)
         sensitive assays)
IT    Receptors
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (ATP-gated; methods for detecting modulators of ion channels using
         thallium (i) sensitive assays)
IT    Potassium channel
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (HERG; methods for detecting modulators of ion channels using thallium
         (i) sensitive assays)
IT    Potassium channel
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (KCNQ; methods for detecting modulators of ion channels using thallium
         (i) sensitive assays)
IT    Potassium channel
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (Maxi-K; methods for detecting modulators of ion channels using
         thallium (i) sensitive assays)
IT    Glutamate receptors
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (NMDA-binding; methods for detecting modulators of ion channels using
         thallium (i) sensitive assays)
IT    Potassium channel
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (SK(small conductance Ca2+ activated); methods for detecting modulators
         of ion channels using thallium (i) sensitive assays)
IT    Capsaicin receptors
      RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
      ANST (Analytical study); BIOL (Biological study)
         (VR1; methods for detecting modulators of ion channels using thallium
         (i) sensitive assays)
IT    Cation channel
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RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(cAMP, cGMP activated; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Ion channel
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(calcium-activated; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Transport proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(calcium-sodium exchanger; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(channel-linked; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Buffers
(chloride-free; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Transport properties
(ionic; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Glutamate receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(kainate; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Glutamate receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(metabotropic; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Animal tissue culture
Culture media
Drug screening
Fluorescence quenching
Fluorescent substances
Genetic methods
Ionophores
Mammalia
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 5-HT receptors
Capsaicin receptors
Cholinergic receptors
Dopamine receptors
G protein-coupled receptors
Inositol 1,4,5-trisphosphate receptors
Ion channel
Ryanodine receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Amino acids, biological studies

Vitamins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(nicotinic acetylcholine-gated; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT Ion channel
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(voltage gated; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 5398-34-5, ANTS
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(ANTS; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 411209-52-4, Fluo 4FF pentapotassium salt
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Fluo 4FF pentapotassium salt; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 411209-53-5, FluoZin 1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(FluoZin 1; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 170516-42-4, Phen Green
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Phen Green; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 7447-40-7, Potassium chloride, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ion co-transporters for; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 50-67-9, Serotonin, analysis 51-61-6, Dopamine, analysis 56-86-0, Glutamic acid, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(ion transporters for; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 24345-16-2, Apamin
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 123632-39-3, Fluo-3 **124549-11-7**, PBFI 154324-80-8, BTC 170516-41-3, Magnesium Green 184228-02-2, Mag-Fura Red 216393-45-2, APTRA-BTC, tripotassium salt 273221-59-3, Fluo-4 411209-54-6, FluoZin 2 tetrapotassium salt
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 16887-00-6, Chloride, uses 20461-54-5, Iodide, uses 24959-67-9, Bromide, uses
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 50-99-7, D-Glucose, biological studies 51-84-3, Acetylcholine,

biological studies 54-11-5, Nicotine 56-85-9, Glutamine, biological studies 144-55-8, Sodium carbonate (NaHCO3), biological studies 299-27-4, Potassium gluconate 299-28-5, Calcium gluconate 300-54-9, Muscarine 462-58-8, Carbamylcholine 527-07-1, Sodium gluconate 3632-91-5, Magnesium gluconate 7365-45-9, HEPES 7440-28-0, Thallium, biological studies 7487-88-9, Sulfuric acid magnesium salt (1:1), biological studies 7558-80-7, Sodium phosphate (NaH2PO4) 14127-61-8, Calcium ion, biological studies 17341-25-2, Sodium ion, biological studies 22537-56-0, biological studies 24203-36-9, Potassium ion, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 71-52-3, Hydrogen carbonate, biological studies 7791-12-0, Thallium chloride 10102-45-1, Thallium nitrate (TlNO3) 12026-06-1, Thallium hydroxide 14996-02-2, Hydrogen sulfate, biological studies 15843-14-8, Thallium acetate
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(methods for detecting modulators of ion channels using thallium (i) sensitive assays)

IT 9000-83-3, ATPase
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(sodium-potassium and proton-potassium activated; methods for detecting modulators of ion channels using thallium (i) sensitive assays)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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(FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1 STRUCTURE UPLOADED
L2 50 S SAM L1
L3 62637 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4 771 S L3 AND RECEPTOR
L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

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L7 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:2850 CAPLUS
DOCUMENT NUMBER: 140:77013
TITLE: Preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia
INVENTOR(S): Jaehne, Gerhard; Frick, Wendelin; Flohr, Stefanie; Lindenschmidt, Andreas; Glombik, Heiner; Kramer, Werner; Heuer, Hubert; Schaefer, Hans-Ludwig
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000804	A1	20031231	WO 2003-EP5815	20030604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10227506	A1	20040108	DE 2002-10227506	20020619
US 2004082561	A1	20040429	US 2003-463807	20030618
PRIORITY APPLN. INFO.:			DE 2002-10227506 A	20020619
			US 2002-411984P P	20020919

OTHER SOURCE(S): MARPAT 140:77013
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2, R3, R4, R5, R6 = (un)substituted alkylene-(LAG)n; n = 1-5; LAG = sugar; amino sugar; amino acid, etc.] and their pharmaceutically acceptable salts were prepared For example, N-alkylation of 1,4-diazabicyclo[2.2.2]octane with benzyl bromide II, e.g., prepared from 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-2-azetidinone and 1,2-bisbromomethylbenzene, afforded diphenylazetidinone III. In rat liver chloresterol absorption assays, 26-examples of compds. I exhibited EC50 values ranging from 0.03-<1.0 (mg/mouse), e.g., the EC50 value of diphenylazetidinone III was 0.3. Compds. I are claimed useful for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:491222 CAPLUS
DOCUMENT NUMBER: 139:69258
TITLE: Preparation of pyrazolopyridine derivatives as Edg-5 **receptor** antagonists
INVENTOR(S): Ozawa, Koichi; Hirata, Kazuyuki; Yamamoto, Kazuhiko
PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan
SOURCE: PCT Int. Appl., 198 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

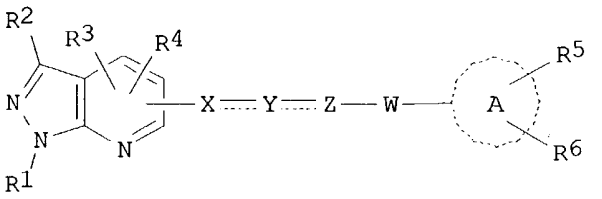
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051876	A1	20030626	WO 2002-JP13059	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,				

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-382398 A 20011214
JP 2002-225343 A 20020801

OTHER SOURCE(S): MARPAT 139:69258

GI



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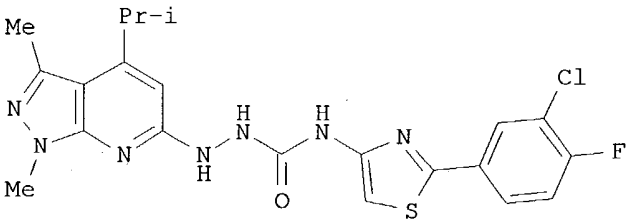


II

AB The title pyrazolopyridine derivs. with general formula of I [wherein R1 = H, (halo)alkyl, (un)substituted aryl, aralkyl, or COR7; R7 = alkyl, alkoxy, (un)substituted aryl, aralkyl, aryloxy, or aralkyloxy; R2 = H, (un)substituted alkyl, or aryl; R3 = H, alkoxy, alkoxy-CO, haloalkyl, cycloalkyl, (un)substituted alkyl, or aryl; R4 = H or (un)substituted alkyl; R5 = H, (cyclo)alkyl, alkoxy, alkoxy-CO, carboxy, alkynyl, halo, CN, NO2, haloalkyl, alkylamino, dialkylamino, acyl, OH, (un)substituted aryloxy, aralkyloxy, aryl, aralkyl, heterocyclyl, alkoxyalkyl, or CONHR8; R8 = (un)substituted aryl or aralkyl; R6 = H, (cyclo)alkyl, alkoxy, alkoxy-CO, carboxy, alkynyl, halo(alkyl), CN, NO2, alkylamino, dialkylamino, acyl, OH, (un)substituted aryloxy, aralkyloxy, aryl, aralkyl, heterocyclyl, alkoxyalkyl, or CONHR8; X = O, -N=, -CH=, (un)substituted -NH-, or -CH2-; Y = =N-, -CH2-, =CH-, -O-, -CO-, a bond, or (un)substituted -NH-; Z = CO, CS, CH2, O, or a bond; W = O, CO, CONH, CH2, NHCH2, a bond, or (un)substituted -NH-; ring A = aryl, heterocyclyl, or cycloalkyl] and prodrugs and pharmaceutically acceptable salts thereof are prepared For example, the compound II was prepared in a multi-step synthesis. II showed IC50 of 0.014 μM against hAGR16 in cow. I act specifically on endothelial differentiation sphingolipid **G-protein**-coupled (Edg) 5 which is a sphingosine-1-phosphate **receptor** and, therefore, are useful as remedies for fibrosis, arteriosclerosis, coronary vasospasm, asthma, nephritis, nerve disorder, peripheral nerve disorder, rheumatoid arthritis, systemic lupus erythematosus (SLE), cancer, etc.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:42372 CAPLUS
DOCUMENT NUMBER: 138:102021
TITLE: cDNAs encoding human olfactory cyclic nucleotide gated (CNG) channel subunits for use in enhancing smell receptors
INVENTOR(S): Zoller, Mark T.; Xu, Hong; Staszewski, Lena; Moyer, Bryan; Pronin, Alexy; Adler, Jon Elliott; Servant, Guy; Callamaras, Nicholas
PATENT ASSIGNEE(S): Senomyx, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004611	A2	20030116	WO 2002-US21184	20020708
WO 2003004611	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003228633	A1	20031211	US 2002-189507	20020708
EP 1414940	A2	20040506	EP 2002-765797	20020708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:
US 2001-303140P P 20010706
US 2001-337154P P 20011210
WO 2002-US21184 W 20020708

AB The present invention relates to isolated nucleic acid sequences that encode human olfactory cyclic nucleotide gated (CNG) channel subunits, and the corresponding polypeptides. The invention further relates to the use of human CNG channels to profile, screen for, and identify compds. that modulate the human olfactory CNG channel. More specifically, the invention relates to the expression of the human olfactory CNG channel in cells, preferably mammalian cells, and the use of these cells in high throughput cell-based assays to identify compds. that enhance or block human olfactory CNG function. Compds. that activate the olfactory CNG channel will enhance smell and can be used to make foods more palatable for individuals with attenuated olfactory function. Conversely, compds. that inhibit the olfactory CNG channel will inhibit smell and can be use to block malodors. Addnl., the invention relates to the use of cell-based olfactory CNG channel assays to identify modulators of **G-protein** coupled **receptor** (GPCRs) and other proteins that regulate cyclic nucleotide levels. Claimed sequence ID#4 is missing.

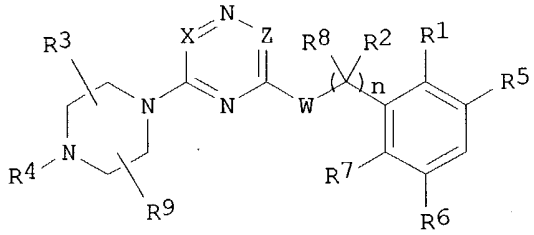
L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:5937 CAPLUS
DOCUMENT NUMBER: 138:73273
TITLE: Preparation of [1,2']bipyrazinyl 5-HT2 **receptor** ligands for treatment of sexual dysfunction
INVENTOR(S): Chiang, Yuan-Ching Phoebe; Dasilva-Jardine, Paul

Andrew; Garigipati, Ravi S.; Guzman-Perez, Angel;
Novomisle, William Albert; Welch, Willard Mckowan
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000666	A1	20030103	WO 2002-IB2293	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003105106	A1	20030605	US 2002-156884	20020528
US 2003125334	A1	20030703	US 2002-163881	20020605
NZ 529542	A	20031219	NZ 2002-529542	20020617
NZ 529543	A	20031219	NZ 2002-529543	20020617
EP 1401820	A1	20040331	EP 2002-735869	20020617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200400026	A	20040615	EE 2004-26	20020617
BR 2002010471	A	20040810	BR 2002-10471	20020617

PRIORITY APPLN. INFO.: US 2001-299953P P 20010621
WO 2002-IB2293 W 20020617

OTHER SOURCE(S): MARPAT 138:73273
GI



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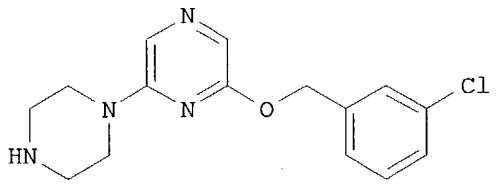


II

AB Title compds. (I) [wherein X and Z = independently CR; R = H, halo, alkyl(amino), or amino; W = O, S, NH, alkylamino, or acetylamino; at least one of R1, R5, R6, or R7 = independently halo, NO2, (alkyl)amino, CN, CONH2, (halo)alkyl, or alkoxy; or C2R1R5 = 5- or 6-membered aromatic or fused ring; or R1 taken together with R2 or R8 forms a 5- or 6-membered fused

ring; R2 and R8 = independently H or (cyclo)alkyl; n = 0-2; R3 and R9 = independently H, halo, alkyl, or alkyl substituted with OH, F, or alkoxy; R4 = H, OH, (hydroxy)alkyl, cyanoalkyl, alkylcarbonyl, alkoxy(carbonyl), or alkenyl; or N-oxides, prodrugs, pharmaceutically acceptable salts, solvates, or hydrates thereof] were prepared as 5-hydroxytryptamine (5-HT) **receptor** ligands, in particular 5-HT2C **receptor** ligands. For instance, 2,6-dichloropyrazine was coupled with piperazine-1-carboxylic acid tert-Bu ester using Na2CO3 in t-BuOH to give 6'-chloro-2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-carboxylic acid tert-Bu ester. Substitution with 3-chlorobenzyl alc. in the presence of KOH and 18-crown-6 in toluene followed by deesterification afforded 6'-(3-chlorobenzyloxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl (II). Compds. of the invention demonstrated affinity at the serotonin 5HT2A and 5HT2C binding sites with Ki values ranging from 0.5 nM to 1.0 μM and 0.1 nM to 586.5 nM, resp. In a functional assay using 5-HT2C expressed NIH 3T3 cells, II displayed EC50 ≤ 1.0 μM. I and pharmaceutical compns. containing I are useful for the treatment of diseases linked to the activation of 5-HT2 receptors, such as sexual dysfunction (no data).

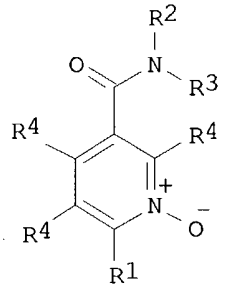
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:521710 CAPLUS
DOCUMENT NUMBER: 137:93690
TITLE: Preparation of nicotinanilide-N-oxides as **G-protein**-coupled **receptor** antagonist for the treatment of inflammation due to neutrophil chemotaxis
INVENTOR(S): Cutshall, Neil S.; Yager, Kraig M.
PATENT ASSIGNEE(S): Darwin Discovery Ltd., UK
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002053544	A1	20020711	WO 2001-US47543		20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003004189	A1	20030102	US 2001-15861		20011212
PRIORITY APPLN. INFO.:			US 2000-258730P	P	20001229

OTHER SOURCE(S): MARPAT 137:93690
GI



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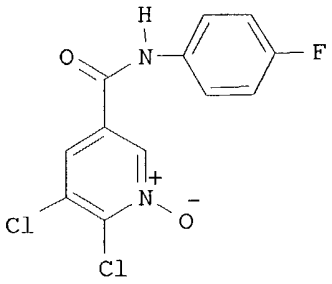


II

AB Title compds. I, their optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts [wherein: R1 = R5, R5-heteroalkylene; R5 = H, halo, alkyl, heteroalkyl, etc.; R2, R3 = H, alkyl, heteroalkyl, aryl, etc.; R4 = H, halo, alkyl, heteroalkyl, etc.] were claimed. For example, hydrogen peroxide mediated N-oxidation of 2-chloro-N-(4-fluorophenyl)-6-methylnicotinamide provided claimed oxynicotinamide II in 10% yield. Nicotinanilide N-oxides I are disclosed to inhibit chemokine-mediated cellular and inflammation events. Specific binding of 95 claimed examples to human interleukin 8 and human growth-regulatory oncogene-α (GRO-α) chemokine were reported as < or > 40% at 20 μM ligand concentration, e.g., compound II > 40% for GRO-α, were disclosed. Also, the specific binding of 9 claimed examples to human chemokine CCR5, human interleukin-CXCR1, human interleukin-CXCR2, human neuropeptide Y1 and somatostatin, e.g., compound II: < 40% for CCR5, somatostatin; > 40% for CXCR1, CXCR2; no data for NYP1, were disclosed. A method for the identification of nicotinanilide-N-oxides. I receptors from cell or cellular components and the isolation of compds. I which bind to TNF-α signaling proteins via affinity bead chromatog. and surface plasmon resonance (SPR) are claimed (no data).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:293976 CAPLUS
DOCUMENT NUMBER: 136:321701
TITLE: Methods for detecting modulators of ion channels using thallium (i) sensitive assays
INVENTOR(S): Weaver, Charles David
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002031508	A1	20020418	WO 2001-US32132	20011012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002015350	A5	20020422	AU 2002-15350	20011012

US 2002168625 A1 20021114 US 2001-975891 20011012
EP 1327150 A1 20030716 EP 2001-983962 20011012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2000-240523P P 20001013
WO 2001-US32132 W 20011012

AB The invention concerns novel thallium-sensitive assays for identifying modulators of ion channels, channel-linked receptors or ion transporters are provided. The invention further provides novel chloride-free buffers and low chloride cell growth media.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:230597 CAPLUS
DOCUMENT NUMBER: 138:1793
TITLE: Development of Gs-selective inhibitory compounds
AUTHOR(S): Nanoff, Christian; Kudlacek, Oliver; Freissmuth, Michael
CORPORATE SOURCE: Institute of Pharmacology, University of Vienna, Vienna, A-1090, Austria
SOURCE: Methods in Enzymology (2002), 344(G Protein Pathways, Part B), 469-480
CODEN: MENZAU; ISSN: 0076-6879
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review on the three types of effects exerted by the active compds., **G protein** α subunits, to determine their usefulness in expts. in intact cells and animals. These effects are the inhibition of GDP release, the inhibition of **receptor-G protein** coupling, and the inhibition of effector regulation. The availability of biochem. assays should help in overcoming the limitation posed by the fact that the compds. are not membrane permeable. The structure of a complex was also solved in which Gαs is bound to a dimer formed by the catalytic domains of adenylyl cyclase. Thus, a structural model is available that may guide the search for improved inhibitors of Gαs. (c) 2002 Academic Press.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:884055 CAPLUS
DOCUMENT NUMBER: 136:227068
TITLE: Pharmacological analysis of CCK2 **receptor** ligands using COS-7 and SK-N-MC cells, expressing the human CCK2 **receptor**
AUTHOR(S): Nilsson, Isabelle; Monstein, Hans-Jurg; Lindstrom, Erik; Hakanson, Rolf; Svensson, Samuel
CORPORATE SOURCE: Division of Pharmacology, Faculty of Health Sciences, University of Linkoping, University Hospital, Linkoping, S-581 85, Swed.
SOURCE: Regulatory Peptides (2002), 103(1), 29-37
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of CCK2 **receptor** ligands were analyzed with respect to their interaction with binding sites in the membranes of COS-7 cells and SK-N-MC cells transiently expressing the human CCK2 **receptor** (short isoform). The ligands were YF476, YM022, AG041R, L-740,093, JB93182, PD134308, and PD136450. Their binding was analyzed by

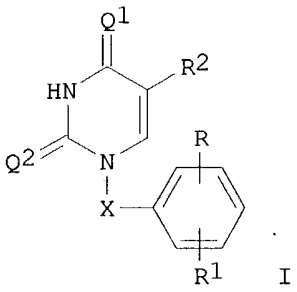
radioligand competition using [3H]L-365,260 as the labeled ligand. Saturation binding anal. indicated that [3H]L-365,260 interacted with a single class of binding sites. In competition binding expts. using COS-7-cell membranes, all seven ligands were incubated together with 2 nM [3H]L-365,260. The data for four of the compds. fitted a one-site model (pKi values: YM022: 9.2; YF476: 9.6; L-740,093: 9.2; and AG041R: 8.3), while the data for the three others fitted a two-site model (pKi values: JB93182: 8.8 and 6.0; PD134308: 9.0 and 6.1; and PD136450: 9.0 and 5.4). SK-N-MC cell membranes and 2 nM [3H]L-365,260 were incubated together with YM022, YF476, JB93182, and PD134308. The data for YM022 and YF476 fitted a one-site model (pKi values: YM022: 9.3; YF476: 9.4), while the data for JB93182 and PD134308 fitted a two-site model (pKi values: JB93182: 8.7 and 6.2; PD134308: 9.1 and 7.0). Competition binding expts. in the presence of the GTP-analog guanylylimidodiphosphate, using either of the two cell types, produced similar binding data for PD134308 and JB93182 as in the absence of GTP-analog. The human **receptor** seems to exist in a low and/or high affinity state. The shift from low to high affinity does not seem to reflect the degree of **G protein** coupling.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:96227 CAPLUS
DOCUMENT NUMBER: 130:153665
TITLE: Preparation of arylpyrimidinediones as P2-purinoceptor 7-transmembrane **G-protein** coupled **receptor** antagonists.
INVENTOR(S): Kindon, Nicholas; Meghani, Premji; Thom, Stephen
PATENT ASSIGNEE(S): Astra Pharmaceuticals Ltd., UK; Astra Aktiebolag
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9905123	A1	19990204	WO 1998-SE1391		19980715
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9883704	A1	19990216	AU 1998-83704		19980715
EP 1000038	A1	20000517	EP 1998-934105		19980715
EP 1000038	B1	20021106			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2001510833	T2	20010807	JP 2000-504122		19980715
AT 227276	E	20021115	AT 1998-934105		19980715
US 6200981	B1	20010313	US 1999-155091		19990921
PRIORITY APPLN. INFO.:			SE 1997-2794	A	19970724
			WO 1998-SE1391	W	19980715

OTHER SOURCE(S): MARPAT 130:153665
GI



I

AB Title compds. [I; X = bond, CH2, (O-interrupted) C1-3 alkylene; R = H, NO2, NH2, dialkylamino, CO2H, CH2OH, halo, alkoxycarbonyl, (substituted) (O-, S-, or N-interrupted) alkyl, etc.; R1 = amino, aminomethyl, carboxymethylaminomethyl, (O-, S-, or N-interrupted) (substituted) alkyl, etc.; R2 = (substituted) fluorenyl, dibenzocycloheptenyl, etc.; Q1, Q2 = O, S], were prepared as P2-purinoceptor 7-transmembrane **G-protein** coupled **receptor** antagonists. Thus, 2',3',5'-tris-O-[(1,1-dimethylethyl)dimethylsilyl]uridine and Me2NCH2CH2NMe2 in THF at -78° were treated with s-BuLi and then with 9-fluorenone in THF followed by stirring overnight at room temperature to give 5-(9-hydroxy-9H-fluoren-9-yl)-2',3',5'-tris-O-[(1,1-dimethylethyl)dimethylsilyl]uridine. The latter was treated with Et3SiH and BF3.Et2O in CH2Cl2 to give a residue which was treated with Bu4NF in THF to give 5-(9H-fluoren-9-yl)uridine. This was refluxed with aqueous HCl in EtOH to give 5-(9H-fluoren-9-yl)-3,4-dihydro-2,4(1H,3H)-pyrimidinedione. Stirring of the latter with Et4NOH and Me 3-bromomethylbenzoate in DMF gave Me 3-[[5-(9H-fluoren-9-yl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]methyl]benzoate. This was refluxed with Lawesson's reagent in THF followed by saponification of the product with LiOH in THF/H2O to give 3-[[5-(9H-fluoren-9-yl)-3,4-dihydro-2-oxo-4-thioxo-1(2H)-pyrimidinyl]methyl]benzoic acid. I bound to P2-purinoceptor 7-transmembrane **G-protein** coupled receptors with pA2 >4.0.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:33926 CAPLUS

DOCUMENT NUMBER: 128:188589

TITLE: Gsα-selective **G protein** antagonists

AUTHOR(S): Hohenegger, M.; Waldhoer, M.; Beindl, W.; Boing, B.; Kreimeyer, A.; Nickel, P.; Nanoff, C.; Freissmuth, M.

CORPORATE SOURCE: Institute of Pharmacology, University of Vienna, A-1090, Austria

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(1), 346-351
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Suramin acts as a **G protein** inhibitor because it inhibits the rate-limiting step in activation of the Gα subunit, i.e., the exchange of GDP for GTP. Here, we have searched for analogs that are selective for Gsα. Two compds. have been identified: NF449 (4,4',4",4'"-[carbonyl-bis[imino-5,1,3-benzenetriyl bis-(carbonylimino)]] tetrakis-(benzene-1,3-disulfonate) and NF503 (4,4'-[carbonylbis[imino-3,1-phenylene-(2,5-benzimidazolylene)carbonylimino]]bis-benzenesulfonate). These compds. (i) suppress the association rate of guanosine

5'-[γ-thio]triphosphate ([35S]GTP[γS]) binding to Gsα-s but not to Giα-1, (ii) inhibit stimulation of adenylyl cyclase activity in S49 cyc- membranes (deficient in endogenous Gsα) by exogenously added (Gsα-s, and (iii) block the coupling of β-adrenergic receptors to Gs with half-maximum effects in the low micromolar range. In contrast to suramin, which is not selective, NF503 and NF449 disrupt the interaction of the A1-adenosine **receptor** with its cognate G proteins (Gi/Go) at concns. that are >30-fold higher than those required for uncoupling of β-adrenergic **receptor** /Gs tandems; similarly, the angiotensin II type-1 **receptor** (a prototypical Gq-coupled **receptor**) is barely affected by the compds. Thus, NF503 and NF449 fulfill essential criteria for Gsα-selective antagonists. The observations demonstrate the feasibility of subtype-selective **G protein** inhibition.

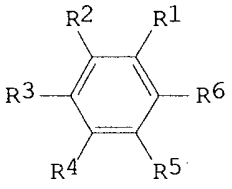
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:603874 CAPLUS
DOCUMENT NUMBER: 119:203874
TITLE: Preparation of aromatic peptidomimetics
INVENTOR(S): Hirschmann, Ralph; Leahy, Ellen; Sprengeler, Paul
PATENT ASSIGNEE(S): University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9312084	A1	19930624	WO 1992-US10694	19921211
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5250564	A	19931005	US 1991-806048	19911212
PRIORITY APPLN. INFO.:			US 1991-806048	19911212

OTHER SOURCE(S): MARPAT 119:203874
GI



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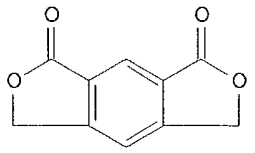

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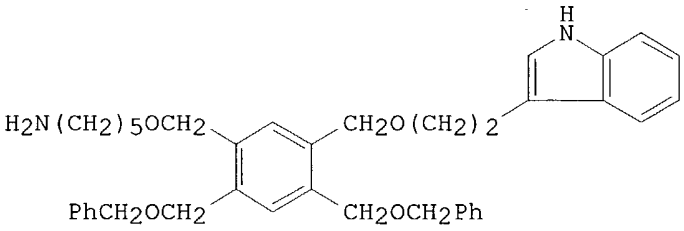

III

AB Title compds. I [R1 = RA(CH2)nOCH2, RA'(CH2)nO2CCH2, RA(CH2)n, RA(CH2)nCOCH2 wherein RA = H, C1-14 alkyl, C1-14 alkenyl and ≤4 N, n = 0-12; R2, R3, R4 = RB(CH2)mOCH2, RB(CH2)mO2CCH2, RB(CH2)m, RB(CH2)mCOCH2, wherein RB = H, C'6-14 aryl, m = 0-5; R5 = RC'NH(CH2)p RD(CH2)p, etc. wherein RC = H, C1-14 alkyl, C1-14 alkenyl, etc.; RD = H, HO, HCO, etc., p = 0-10; R6 = H, HO] or a salt thereof, useful for modulating the activity of at least one mammalian **G-protein**-linked **receptor**, are prepared 1,2,4,5-Tetraformylbenzene in 10N KOH was stirred at room temperature for 5 h to give II which in 7 steps was converted to title compound III. The affinity of I for substance P **receptor** was shown.

L7 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:592173 CAPLUS
DOCUMENT NUMBER: 111:192173
TITLE: Magnesium and cell proliferation
AUTHOR(S): Maguire, Michael E.
CORPORATE SOURCE: Sch. Med., Case Western Reserve Univ., Cleveland, OH, 44106, USA
SOURCE: Annals of the New York Academy of Sciences (1988), 551(Membr. Cancer Cells), 201-17
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Preliminary data using cell-permeable Mg2+ indicators based on tropolone suggest the feasibility of the dynamic and selective determination of intracellular free Mg2+ concentration in mammalian cells. Mg2+-deficient cell lines were also developed. Murine S49 lymphoma cells in normal 0.8 mM Mg2+ medium double in 17 h, but die when placed in 0.2 mM Mg2+ medium. Two classes of S49 clones were isolated which grow in 30 μM Mg2+ with doubling times of 22 and 60 h. Although total cell Mg2+ is decreased by 50%, the decrease is selective, since cytoplasmic Mg2+ is decreased 75%, whereas particulate Mg2+ is unchanged. Hormonal response in the Mg2+-deficient cells is defective. CAMP accumulation in response to β-adrenergic **receptor** activation is decreased >95%. In contrast, the Mg2+-deficient cells lose only .apprx.50% of their response to PGE1 **receptor** activation, retain 50% of their β-receptors, and accumulate cAMP in response to cholera toxin at the wild-type rate. Mg2+ transport also occurs at the wild-type rate, but with a slightly higher affinity, and is not longer hormone-sensitive. Ca2+ content is normal or slightly high. T-lymphocytes isolated from rats made Mg2+-deficient for 8 wk give similar results, indicating that the Mg2+-deficient S49 lymphoma cell clones are a good model for Mg2+-deficiency. Apparently, lack of Mg2+ causes growth abnormalities and leads to markedly altered **receptor-G protein** coupling, but may have less effect on **G-protein** -adenylate cyclase interaction.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	88.28	246.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.90	-11.90

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 17, 2004 (20040917/UP).

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	246.07

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CA SUBSCRIBER PRICE	0.00	-11.90

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004
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FILE COVERS 1907 - 23 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004 (20040922/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L2 50 S SAM L1
L3 62637 S L1 FULL

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L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004

=> s l4 and muscarinic
23368 MUSCARINIC
L8 10 L4 AND MUSCARINIC

=> d scan l8

L8 10 ANSWERS CAPLUS COPYRIGHT 2004 ACS on STN
IC ICM C07C229-60
ICS A61K031-136; A61K031-33; A61P043-00; C07C217-84; C07C217-86; C07C217-70; C07C233-43; C07D239-42; C07D239-46; C07D413-12; C07D409-12; C07D401-12; C07C311-44
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
TI Preparation of aryl aniline β-2 adrenergic **receptor** agonists
ST aryl pyrimidines aniline adrenergic **receptor** agonist prepn
IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonist; combination pharmaceutical; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Lung, disease
(chronic obstructive; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Leukotriene antagonists
Muscarinic antagonists
(combination pharmaceutical; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Parturition
(premature; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Anti-inflammatory agents
Heart, disease
Human
Inflammation
Lung, disease
Nervous system, disease
(preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β2; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT 15826-37-6, Sodium cromoglycate 37205-61-1, Protease inhibitor 69049-74-7, Nedocromil sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT 9025-82-5, Phosphodiesterase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; combination pharmaceutical; preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT **530117-15-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)
IT **530084-30-1P** 530084-38-9P **530084-55-0P**

530084-56-1P 530084-57-2P 530084-58-3P
530084-59-4P 530084-60-7P 530084-61-8P 530084-62-9P
530084-63-0P 530084-64-1P 530084-65-2P 530084-66-3P 530084-87-8P
530084-88-9P **530116-67-7P 530116-69-9P**
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530116-77-9P 530116-79-1P 530116-81-5P
530116-83-7P 530116-85-9P 530116-87-1P **530116-89-3P**
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530117-22-7P 530117-24-9P 530117-26-1P
530117-28-3P 530117-29-4P 530117-30-7P
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530118-14-0P 530118-15-1P 530118-17-3P 530118-19-5P 530118-20-8P
530118-21-9P 530118-22-0P 530118-23-1P 530118-24-2P 530118-25-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)

IT 57-68-1 77-76-9, 2,2-Dimethoxypropane 79-72-1 92-67-1, 4-Aminobiphenyl 98-80-6, Phenylboronic acid 100-52-7, Benzaldehyde, reactions 104-96-1, 4-(Methylthio)aniline 144-83-2 312-35-6, 4-[(4-Fluorophenyl)sulfonyl]aniline 461-82-5, 4-(Trifluoromethoxy)aniline 587-02-0, 3-Ethylaniline 619-45-4, Methyl 4-aminobenzoate 651-06-9 1127-45-3, 8-Hydroxyquinoline-N-oxide 1679-18-1, 4-Chlorophenylboronic acid 1783-81-9, 3-(Methylthio)aniline 2316-64-5, 5-Bromo-2-hydroxybenzyl alcohol 4534-11-6, 3-Methyl-4-isopropylaniline hydrochloride 5197-28-4, 2-Bromo-4-nitroanisole 5470-49-5, 4-(Methylsulfonyl)aniline 6315-89-5, 3,4-Dimethoxyaniline 6336-68-1 6973-47-3 7019-01-4, 4-(Phenylsulfonyl)aniline 7146-68-1, 4-(4-Chlorobenzenesulfonyl)phenylamine 7525-23-7 13472-00-9, 4-Aminophenethylamine 21626-70-0 24313-88-0, 3,4,5-Trimethoxyaniline 26815-49-6, 3-Aminodiphenyl sulfone 51123-09-2 51388-20-6, 4-Benzyloxyaniline hydrochloride 51628-12-7, 4-Iodophenylacetonitrile 63503-60-6, 3-Chlorophenylboronic acid 73918-56-6, 4-Bromophenethylamine 75705-21-4, 4-(Aminomethyl)phenylboronic acid hydrochloride 76590-35-7, 4-(o-Tolylthio)aniline 78191-00-1, N-Methyl-N-methoxyacetamide 83527-99-5 92028-21-2, 4-Methoxy-3-phenylaniline hydrochloride 92903-03-2, 4-Amino-2-cyclohexylphenol 114306-97-7 135884-31-0 146631-00-7, 4-Benzyloxyphenylboronic acid 150255-96-2, 3-Cyanophenylboronic acid 175136-34-2 397242-08-9, 4-[(4-Methylpyrimidin-2-yl)thio]benzeneamine 530118-81-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aryl aniline β-2 adrenergic **receptor** agonists for treatment of pulmonary disorders)

IT 15450-72-3P, 8-Acetoxy-2(1H)-quinolinone 19434-42-5P 52113-69-6P 54030-34-1P 62978-73-8P, 5-Acetyl-8-hydroxy-2(1H)-quinolinone 73918-57-7P, 4-Iodophenethylamine 93609-84-8P, 5-Acetyl-8-benzyloxy-

2(1H)-quinolinone 100331-89-3P 102293-80-1P 530084-67-4P
530084-68-5P 530084-69-6P 530084-71-0P **530084-72-1P**
530084-74-3P 530084-75-4P 530084-76-5P 530084-77-6P 530084-78-7P
530084-80-1P 530084-81-2P 530084-82-3P 530084-84-5P 530118-35-5P
530118-37-7P 530118-41-3P **530118-42-4P 530118-47-9P**
530118-49-1P 530118-52-6P 530118-61-7P 530118-63-9P 530118-65-1P
530118-66-2P 530118-68-4P 530118-70-8P, 2-(3-Cyanophenyl)-4-
nitroanisole 530118-72-0P, 3-(3-Cyanophenyl)-4-methoxyaniline
530118-75-3P, 2-(4-Aminomethylphenyl)-4-nitroanisole 530118-76-4P,
2-(3-Chlorophenyl)-4-nitroanisole 530118-78-6P, 3-(3-Chlorophenyl)-4-
methoxyaniline 530118-80-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of aryl aniline β-2 adrenergic **receptor** agonists
for treatment of pulmonary disorders)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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(FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1 STRUCTURE UPLOADED
L2 50 S SAM L1
L3 62637 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4 771 S L3 AND RECEPTOR
L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004
L8 10 S L4 AND MUSCARINIC

=> d ibib abs 18 1-10

L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:703125 CAPLUS
TITLE: Preparation of biphenyl derivatives as β2-adrenergic agonists and **muscarinic** antagonists for pulmonary disorders.
INVENTOR(S): Mammen, Mathai; Dunham, Sarah; Hughes, Adam; Lee, Tae Weon; Husfeld, Cralg; Stangeland, Eric
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167167	A1	20040826	US 2004-779157	20040213
WO 2004074276	A1	20040902	WO 2004-US4224	20040213

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,

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WO 2004074812 A2 20040902 WO 2004-US4273 20040213

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WO 2004074246 A2 20040902 WO 2004-US4449 20040213

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GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-447843P P 20030214
US 2003-467035P P 20030501

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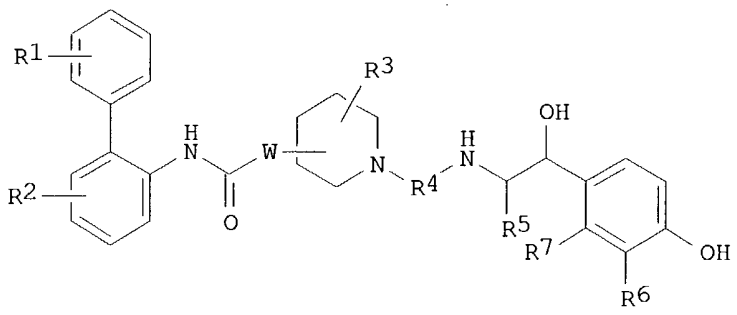

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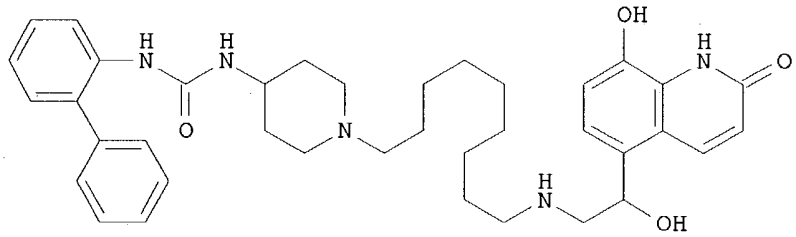

II

AB Title compds. I [R1 (taken 0-3 times) = alk(en/yn)yl, cycloalkyl, etc.; R2 (taken 0-3 times) = alk(en/yn)yl, cycloalkyl, CN, etc.; W = O, substituted N; R3 (taken 0-4 times) = alk(en/yn)yl, cycloalkyl, etc.; R4 = divalent group; R5 = H, alkyl; R6 = amino, alkoxy, etc.; R7 = H, etc.] are prepared For instance, N-[1,1'-Biphenyl-2-yl]-N'-[1-(9-aminononyl)piperidin-4-yl]urea (preparation given) is combined with 8-Benzyloxy-5-(2,2-dihydroxyacetyl)-1H-quinolin-2-one (CH2Cl2, NaHB(OAc)3) and the product reduced (MeOH, H2-Pd/C) to give II. Selected example compds. have Ki < 10 nM for the β2 and **muscarinic receptor**. I are useful in the treatment of pulmonary disorders, such as chronic obstructive pulmonary disease and asthma.

L8 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:656585 CAPLUS
DOCUMENT NUMBER: 139:197373
TITLE: Nicotinamide PDE4 inhibitors in combination with tiotropium **muscarinic receptor** antagonists for treating inflammatory, allergic and respiratory diseases
INVENTOR(S): Bailey, Simon; Gautier, Elisabeth Colette Louise; Henderson, Alan John; Mathias, John Paul; McLeod, Dale Gordon; Monaghan, Sandra Marina; Stammen, Blanda Luzia Christa
PATENT ASSIGNEE(S): Pfizer Limited, UK; Magee, Thomas Victor; Marfat, Anthony; Pfizer Inc.; et al.
SOURCE: PCT Int. Appl., 254 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068233	A1	20030821	WO 2003-IB378	20030203

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003220361	A1	20031127	US 2003-360100	20030206
US 2003220366	A1	20031127	US 2003-361062	20030206

PRIORITY APPLN. INFO.:

GB 2002-3196	A	20020211
GB 2002-20984	A	20020910
GB 2002-24454	A	20021021
GB 2002-27140	A	20021120
US 2002-361991P	P	20020305
GB 2002-20999	A	20020910
US 2002-414247P	P	20020926
US 2002-414304P	P	20020926
GB 2002-24453	A	20021021
US 2002-425406P	P	20021112
US 2002-425474P	P	20021112
GB 2002-27139	A	20021120
US 2002-433330P	P	20021213
US 2002-433336P	P	20021213

OTHER SOURCE(S): MARPAT 139:197373

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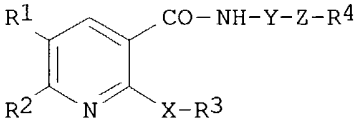

I

AB The invention relates to a combination of nicotinamides (shown as I; variables defined below; e.g. anti-2-(benzo[1,3]dioxol-5-yloxy)-N-[4-(2-hydroxybenzoylamino)cyclohexyl]nicotinamide) and tiotropium or a derivative thereof, compns. containing them and the uses of, such combinations. The nicotinamide derivs. according to the present invention are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic, respiratory diseases, disorders and conditions, as well as wounds. For I: R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-, -S- or -NH-; R3 = Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl or the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = 4-HNcyclohexyl, piperidin-1,4-diyl, 8-azabicyclo[3.2.1]octane-3,8-diyl, and 4-R5Ncyclohexyl wherein in each the N is bonded to Z in I and R5 = (C1-C4)alkyl and phenyl(C1-C4)alkyl. Z = C(O), C(O)NH, SO2, SO2NH, C(O)CH2NHSO2, SO2NHC(O), C(O)CH2NHC(O) wherein the left end is bonded to Y and the other end to R4; or alternatively Y-Z together = 4-NHC(O)cyclohexyl; R4 = Ph, naphthyl heteroaryl and (C3-C8)cycloalkyl, (un)substituted (C1-C6)alkyl; addnl. details including provisos are given in the claims. The antiinflammatory properties of 72 examples of I are demonstrated by their ability to inhibit TNFα release from human peripheral blood mononuclear cells, e.g. IC50 = 0.014 nM for syn-2-(3,4-difluorophenoxy)-5-fluoro-N-[4-(2-hydroxy-5-methylbenzoylamino)cyclohexyl]nicotinamide. About 200 example prepns. of I and 75 of intermediates, the same as in WO 03/068235 A1, are included.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:506580 CAPLUS
DOCUMENT NUMBER: 139:79178
TITLE: Synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivatives and use as phosphodiesterase VII inhibitors and in combination with other agents
INVENTOR(S): Eggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10163991	A1	20030703	DE 2001-10163991	20011224
WO 2003055882	A1	20030710	WO 2002-EP12533	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1458722	A1	20040922	EP 2002-805744	20021108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: DE 2001-10163991 A 20011224
WO 2002-EP12533 W 20021108
OTHER SOURCE(S): MARPAT 139:79178

AB The invention concerns the synthesis of 3H-pyrrolo[2,3-d]pyrimidine derivs., their physiol. acceptable salts, stereoisomers, solvates, mixts. thereof and their use as phosphodiesterase VII inhibitors in the treatment of diseases that are influenced by the phosphodiesterase VII regulation of human eosinophil activation and degranulation. Osteoporesis, tumors, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, AIDS, autoimmune and heart diseases can be treated with the drugs. Thus the synthesis of 5-isopropyl-4-oxo-7-p-tolyl-4,7-dihydro-3H-pyrrolo[2,3-d]pyrimidine-6-carboxylic acid Et ester and analog compds. is described along with injection, suppository, tablet and other formulations.

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:396843 CAPLUS
DOCUMENT NUMBER: 138:401502
TITLE: Preparation of aryl aniline β-2 adrenergic **receptor** agonists
INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Leadbetter, Michael R.; Nodwell, Matthew B.; Trapp, Sean G.; Aggen, James; Church, Timothy J.
PATENT ASSIGNEE(S): Theravance, Inc, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042164	A1	20030522	WO 2002-US36237	20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1446379	A1	20040818	EP 2002-780622	20021112
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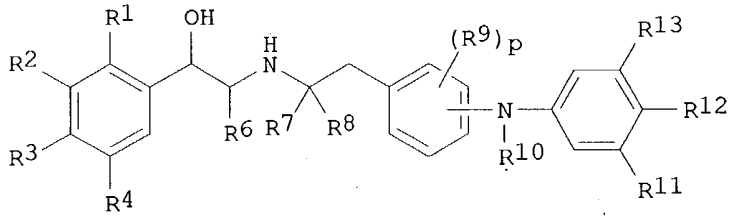
US 2004059116	A1	20040325	US 2003-642926	20030818
PRIORITY APPLN. INFO.:			US 2001-338194P	P 20011113
			US 2001-343771P	P 20011228
			US 2002-292211	A1 20021112
			WO 2002-US36237	W 20021112

OTHER SOURCE(S): MARPAT 138:401502
GI



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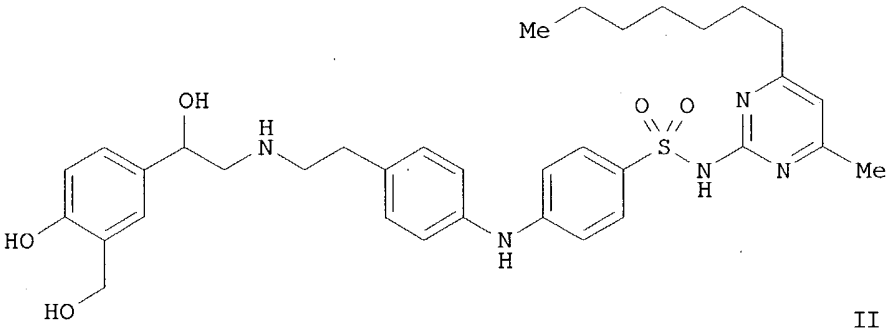


II

AB Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (hetero)aryl, etc.; R10 = H, alkyl; R11-13 = H, (cyclo)alkyl, alkenyl,

alkynyl, (hetero)aryl, etc.; p = 0-4] are prepared For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-α-bromoacetophenone (preparation given) is reacted with 4-bromophenethylamine (CH2Cl2, Et3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimidinyl)sulfanilamide (PhMe, dppf, Pd2dba3, 80°, 5 h) and then deprotected with HOAc (80°, 5 h) to give II. All of the compds. tested demonstrated greater binding at the β2 adrenergic **receptor** than at the β1 adrenergic **receptor**, i.e., Ki(β1) > Ki(β2); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

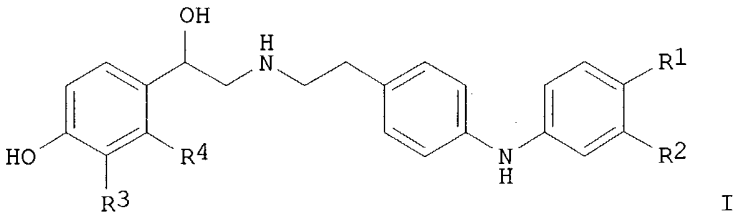
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:396839 CAPLUS
DOCUMENT NUMBER: 138:401501
TITLE: Preparation of aryl aniline β-2 adrenergic **receptor** agonists
INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Aggen, James
PATENT ASSIGNEE(S): Theravance, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003042160	A1	20030522	WO 2002-US36188		20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003153597	A1	20030814	US 2002-292211		20021112
US 6653323	B2	20031125			
US 2004059116	A1	20040325	US 2003-642926		20030818
PRIORITY APPLN. INFO.:			US 2001-338194P	P	20011113
			US 2002-292211	A1	20021112

OTHER SOURCE(S): MARPAT 138:401501
GI



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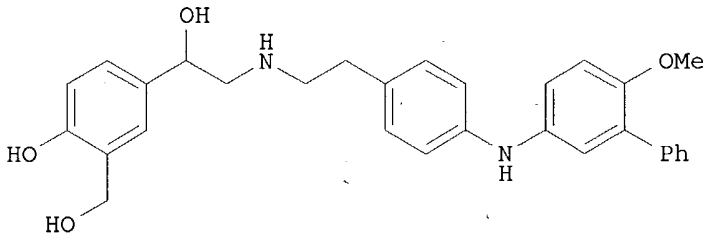

II

AB Title compds. I [R1 = methoxy, ethoxy; R2 = H, Ph or R1 = H and R2 = phenyl; R3 = CH2OH, NHCHO; R4 = H or R3-4 = taken together are NHC(O)CH=CH] are prepared For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-α-bromoacetophenone (preparation given) is reacted with 4-bromophenethylamine (CH2Cl2, Et3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with 4-methoxy-3-phenylaniline (PhMe, dppf, Pd2dba3, NaOBu-t, 80°, 5 h) and then deprotected with HOAc (80°, 5 h) to give II. All of the compds. tested demonstrated greater binding at the β2 adrenergic **receptor** than at the β1 adrenergic **receptor**, i.e., Ki(β1) > Ki(β2); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:282532 CAPLUS
DOCUMENT NUMBER: 138:287681
TITLE: Preparation of heteroaryl substituted tetrazole modulators of metabotropic glutamate **receptor** -5
INVENTOR(S): Cosford, Nicholas D.; Roppe, Jeffrey; Chen, Chixu; Smith, Nicholas; Reger, Thomas
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029210	A2	20030410	WO 2002-US31294	20021001
WO 2003029210	A3	20031120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1434773 A2 20040707 EP 2002-776076 20021001

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

WO 2004030637 A2 20040415 WO 2003-US9717 20030331

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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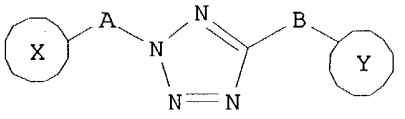
PRIORITY APPLN. INFO.: US 2001-327132P P 20011004
WO 2002-US31294 W 20021001
WO 2002-US40147 A 20021213
WO 2002-US41720 A 20021213
WO 2002-US40237 A 20021216
WO 2002-US40486 A 20021217

OTHER SOURCE(S): MARPAT 138:287681

GI



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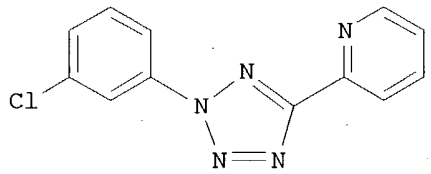

II

AB Title compds. I [X, Y = (un)substituted (hetero)aryl; A, B = alkyl, alkyl-SO-alkyl, alkyl-SO2-alkyl, etc.] are prepared For instance, 2-formylpyridine is condensed with toluenesulfonyl hydrazide to form the hydrazone. 3-Chloroaniline is converted to the diazonium salt and reacted with the hydrazone to form 2-[2-(3-chlorophenyl)-2H-tetrazol-5-yl]pyridine (II) as a pale orange solid. Compds. of the invention have IC50 < 10μM for mGluR5 in the calcium flux assay. I are mGluR5 modulators useful in the treatment of psychiatric and mood disorders such as, schizophrenia, anxiety, depression, and panic, as well as in the treatment of pain and other diseases.

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:832576 CAPLUS
DOCUMENT NUMBER: 137:346197
TITLE: Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent
INVENTOR(S): Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony;

Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed

PATENT ASSIGNEE(S): Epigenesis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 764 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085309	A2	20021031	WO 2002-US13143	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004049022	A1	20040311	US 2003-627930	20030725
PRIORITY APPLN. INFO.:			US 2001-286036P	P 20010424
			WO 2002-US13135	A2 20020423
			WO 2002-US13143	A2 20020423

OTHER SOURCE(S): MARPAT 137:346197

AB This patent relates to a composition comprising a carrier, oligonucleotides (oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 **receptor** mRNA, one targeting adenosine A2b **receptor**, and two targeting an A3 **receptor** are capable of countering the effect of exogenously administered adenosine which is mediated by the specific **receptor** they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addition, they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. These agents and the composition and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases associated with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and composition may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:832575 CAPLUS

DOCUMENT NUMBER: 137:346196

TITLE: Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

INVENTOR(S): Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony; Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed

PATENT ASSIGNEE(S): Epigenesis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 872 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085308	A2	20021031	WO 2002-US13135	20020423
WO 2002085308	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XA13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XB13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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WO 2002085308	A2	20021031	WO 2002-XC13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004049022	A1	20040311	US 2003-627930	20030725
PRIORITY APPLN. INFO.:			US 2001-286137P	P 20010424

WO 2002-US13135 A 20020423
WO 2002-US13143 A2 20020423

OTHER SOURCE(S): MARPAT 137:346196

AB This patent relates to a composition comprising a carrier, oligonucleotides (oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 **receptor** mRNA, one targeting adenosine A2b **receptor**, and two targeting an A3 **receptor** are capable of countering the effect of exogenously administered adenosine which is mediated by the specific **receptor** they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addition, they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. Treatment with antisense oligonucleotides in combination with anti-inflammatory steroid and/or ubiquinones is also provided. These agents and the composition and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases associated with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and composition may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:609823 CAPLUS

DOCUMENT NUMBER: 136:95912

TITLE: NF449: a subnanomolar potency antagonist at recombinant rat P2X1 receptors

AUTHOR(S): Braun, Kirsten; Rettinger, Jurgen; Ganso, Matthias; Kassack, Matthias; Hildebrandt, Caren; Ullmann, Heiko; Nickel, Peter; Schmalzing, Gunther; Lambrecht, Gunter

CORPORATE SOURCE: Biocentre Niederursel, Department of Pharmacology, University of Frankfurt, Frankfurt/Main, 60439, Germany

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2001), 364(3), 285-290
CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antagonistic effects of the novel suramin analog 4,4',4'',4'''-(carbonylbis(imino-5,1,3-benzenetriylbis(carbonylimino)))tetrakis-benzene-1,3-disulfonic acid (NF449) were studied on contractions of the rat vas deferens elicited by α,β-methylene ATP (αβmeATP; mediated by P2X1 receptors), contractions of the guinea-pig ileal longitudinal smooth muscle elicited by αβmeATP (mediated by P2X3 receptors) or adenosine 5'-O-(2-thiodiphosphate) (ADPβS; mediated by P2Y1 receptors), ATP-induced increases of [Ca2+]i in human embryonic kidney (HEK) 293 cells (mediated by P2Y2 receptors), inward

currents evoked by ATP in follicle cell-free Xenopus laevis oocytes expressing rP2X1 or rP2X3 receptors and degradation of ATP by ecto-nucleotidases in folliculated Xenopus laevis oocytes. In addition, NF449 was examined for its P2 **receptor** specificity in rat vas deferens (α1A-adrenoceptors) and guinea-pig ileum (histamine H1 and **muscarinic** M3 receptors).At native (pIC50=7.15) and recombinant (pIC50=9.54) P2X1 receptors, NF449 was a highly potent antagonist. The P2X3 receptors present in guinea-pig ileum (pIC50=5.04) or expressed in oocytes (pIC50≈5.6) were much less sensitive for NF449. It also was a very weak antagonist at P2Y1 receptors in guinea-pig ileum (pIC50=4.85) and P2Y2 receptors in HEK 293 cells (pIC50=3.86), and showed very low inhibitory potency on ecto-nucleotidases (pIC50≤3.5). NF449 (100 μM) did not interact with α1A-adrenoceptors or histamine H1 and **muscarinic** M3 receptors. Thus, the antagonism by NF449 is highly specific for P2 receptors. In conclusion, the subnanomolar potency at rP2X1 receptors and the rank order of potency, P2X1 >> P2X3 > P2Y1 > P2Y2 > ecto-nucleotidases, make NF449 unique among the P2 **receptor** antagonists reported to date. NF449 may fill the long-standing need for a P2X1-selective radioligand.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:832187 CAPLUS

DOCUMENT NUMBER: 134:147471

TITLE: A potent, long-acting, orally active (2R)-2-[(1R)-3,3-difluorocyclopentyl]-2-hydroxy-2-phenylacetamide: a novel **muscarinic** M3 **receptor** antagonist with high selectivity for M3 over M2 receptors

AUTHOR(S): Mitsuya, Morihiro; Kobayashi, Kensuke; Kawakami, Kumiko; Satoh, Atsushi; Ogino, Yoshio; Kakikawa, Taro; Ohtake, Norikazu; Kimura, Toshifumi; Hirose, Hiroyasu; Sato, Akio; Numazawa, Tomosige; Hasegawa, Takuro; Noguchi, Kazuhito; Mase, Toshiaki

CORPORATE SOURCE: Banyu Tsukuba Research Institute in Collaboration with Merck Research Laboratories, Tsukuba, Ibaraki, 300-2611, Japan

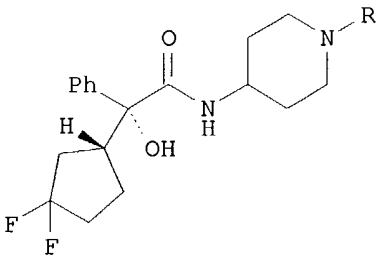
SOURCE: Journal of Medicinal Chemistry (2000), 43(26), 5017-5029
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



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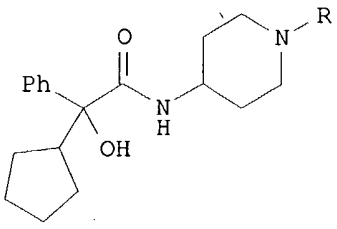
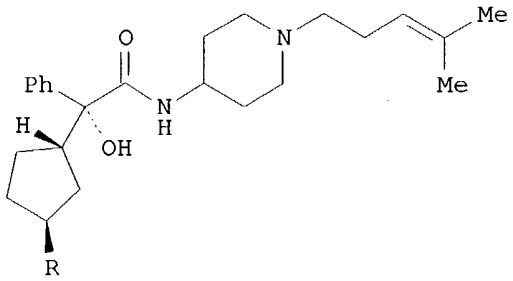


II



III

AB A novel series of (2R)-2-[(1R)-3,3-difluorocyclopentyl]-2-hydroxy-2-phenylacetamides I (R = CH2Ph, 3-furylmethyl, 2-pyridyl, etc.) and II (R = 2-MeC6H4CH2, cyclohexylmethyl, 3-pyridylmethyl, etc.) was designed and synthesized based on the structure and biol. profiles of an active metabolite III (R = OH) of the prototype **muscarinic** M3 **receptor** selective antagonist III (R = H), to develop a potent, long-acting, orally active M3 antagonist for the treatment of urinary tract disorders, irritable bowel syndrome, and respiratory disorders. Investigation of I [R = (substituted phenyl)methyl, (substituted pyridyl)methyl, (substituted thienyl)methyl] containing a Ph or heterocyclic ring as the piperidinyl side chain in place of the 4-methyl-3-pentenyl moiety of I (R = 4-Me-3-pentenyl) revealed that this acid moiety was a versatile template for improving the selectivity for M3 over M2 receptors in comparison with the corresponding cyclopentylphenylacetic acid group. However, since the in vitro metabolic stability of these analogs was insufficient compared with that of III (R = OH), further derivatization was performed by introducing an appropriate hydrophilic group into the Ph or 2-pyridyl ring. Thus, the 1-(6-aminopyridin-2-ylmethyl)piperidine analog I (R = 6-amino-2-pyridylmethyl) exhibiting 190-fold selectivity for M3 receptors (Ki = 2.8 nM) over M2 receptors (Ki = 530 nM) in a human binding assay and good in vitro metabolic stability in dog and human hepatic microsomes was identified. This compound has excellent oral activity at 4 h after oral dosing (1 mg/kg), inhibiting methacholine-induced bronchoconstriction in dogs, and may be useful in clin. situations in which M3 over M2 selectivity is desirable.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004

L1 STRUCTURE UPLOADED

L2 50 S SAM L1

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L3        62637 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4          771 S L3 AND RECEPTOR
L5           73 S L4 AND LIGAND
L6            5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7           12 S L4 AND G (3W) PROTEIN

     FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

     FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004
L8           10 S L4 AND MUSCARINIC

=> s l5 not l6
L9           68 L5 NOT L6

=> s l9 not l7
L10          64 L9 NOT L7

=> s l10 not l8
L11          61 L10 NOT L8

=> t ti l11 1-30

L11  ANSWER 1 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Synthesis, in vitro pharmacology, structure-activity relationships, and
     pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-
     dicarboxylic acid derivatives as potent and selective group II
     metabotropic glutamate receptor antagonists

L11  ANSWER 2 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   [3H]A-317491, a novel high-affinity non-nucleotide antagonist that
     specifically labels human P2X2/3 and P2X3 receptors

L11  ANSWER 3 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Dye-Labeled Benzodiazepines: Development of Small Ligands for
     Receptor Binding Studies Using Fluorescence Correlation
     Spectroscopy

L11  ANSWER 4 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Fluorescent ligands and measuring of binding of samples to androgen
     receptor

L11  ANSWER 5 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of 4-(phenylpiperazinylmethyl)benzamides for treatment of pain
     or gastrointestinal disorders

L11  ANSWER 6 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Ligands for the peroxisome proliferator-activated receptor

L11  ANSWER 7 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of a novel diphosphine-palladium macrocyclic complex
     possessing a molecular recognition site. Oxidative addition studies

L11  ANSWER 8 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Rational Design and Synthesis of Androgen Receptor-Targeted
     Nonsteroidal Anti-Androgen Ligands for the Tumor-Specific Delivery of a
     Doxorubicin-Formaldehyde Conjugate

L11  ANSWER 9 OF 61  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   2', 3'-O-(2,4,6, trinitrophenyl)-ATP and A-317491 are competitive
     antagonists at a slowly desensitizing chimeric human P2X3 receptor
```

L11 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of pyridones as modulators of nuclear receptors, including liver X **receptor** (LXR).

L11 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Novel fluorescence based **receptor** binding assay method for receptors lacking **ligand** conjugates with preserved affinity: Study on estrogen **receptor** α

L11 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI A novel strapped porphyrin **receptor** for molecular recognition

L11 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthetic Inhibitors of Proline-Rich **Ligand**-Mediated Protein-Protein Interaction: Potent Analogs of UCS15A

L11 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of piperidino cannabinoid **receptor** ligands

L11 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of benzotriazepines as gastrin and cholecystokinin **receptor** ligands for treating gastrointestinal disorders

L11 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Exponential pattern recognition-based cellular targeting, compositions, methods and anticancer applications

L11 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and Investigation of New Macrocyclic Diphosphine-Palladium(0) Complexes Based on the Barbiturate Binding **Receptor**

L11 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Anion-Templated Rotaxane Formation

L11 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Refinement and evaluation of a pharmacophore model for flavone derivatives binding to the benzodiazepine site of the GABAA **receptor**

L11 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Environment and mobility of a series of fluorescent reporters at the amino terminus of structurally related peptide agonists and antagonists bound to the cholecystokinin **receptor**

L11 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of naphthalene derivatives as cannabinoid CB1 **receptor** ligands.

L11 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Comparative binding energy (COMBINE) analysis of human neutrophil elastase inhibition by pyridone-containing trifluoromethylketones

L11 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of imidazoles as gastrin and cholecystokinin **receptor** ligands for treatment of gastrointestinal disorders

L11 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and pharmaceutical compositions of gastrin/cholecystokinin **receptor** ligands with proton pump inhibitors

L11 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Analysis of fluorescently labeled substance P analogs: binding, imaging

and **receptor** activation

L11 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Validation of flow cytometric competitive binding protocols and characterization of fluorescently labeled ligands

L11 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Therapeutic uses of PPAR mediators as ABC-1 expression modulators, and preparation thereof

L11 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and characterization of new aromatic tweezers and complex formation with tropylium ion in 1,2-dichloroethane

L11 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 4-(arylhydroxyethylaminoethyl)phenylaminohydroxyethylbenzenes and related compounds as β2 adrenergic **receptor** agonists and partial agonists.

L11 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2004 ACS on STN
TI Nonpeptide cholecystokinin-2 **receptor** agonists

=> d his

(FILE 'HOME' ENTERED AT 20:38:41 ON 23 SEP 2004)

FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1 STRUCTURE UPLOADED
L2 50 S SAM L1
L3 62637 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4 771 S L3 AND RECEPTOR
L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004
L8 10 S L4 AND MUSCARINIC
L9 68 S L5 NOT L6
L10 64 S L9 NOT L7
L11 61 S L10 NOT L8

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5458940 PY>1998
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=> s l11 not l12
L13 15 L11 NOT L12

=> d scan l13

L13 15 ANSWERS CAPLUS COPYRIGHT 2004 ACS on STN
CC 1-6 (Pharmacology)
TI Antimetastatic activities of synthetic Arg-Gly-Asp-Ser (RGDS) and Arg-Leu-Asp-Ser (RLDS) peptide analogs and their inhibitory mechanisms
ST antitumor metastasis RGDS RLDS peptide
IT Basement membrane
Extracellular matrix

(inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Fibronectins
Integrins
Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Adhesion
(bio-, inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Neoplasm inhibitors
(liver, metastasis, inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Neoplasm inhibitors
(lung, metastasis, inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Neoplasm inhibitors
(metastasis, antimetastatic activities of synthetic Arg-Gly-Asp-Ser (RGDS) and Arg-Leu-Asp-Ser (RLDS) peptide analogs and their inhibitory mechanisms)

IT Liver, neoplasm
Lung, neoplasm
(metastasis, inhibitors, inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT Animal growth regulators
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vitronectins, inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser analogs on tumor cell adhesion and antimetastatic activity)

IT 91037-65-9P 150525-67-0P 151997-55-6P **161115-64-6P**
161189-78-2P 173737-87-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antimetastatic activities of synthetic Arg-Gly-Asp-Ser (RGDS) and Arg-Leu-Asp-Ser (RLDS) peptide analogs and their inhibitory mechanisms)

IT 7536-58-5P 160541-40-2P 161189-80-6P 173737-85-4P
173737-86-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antimetastatic activities of synthetic Arg-Gly-Asp-Ser (RGDS) and Arg-Leu-Asp-Ser (RLDS) peptide analogs and their inhibitory mechanisms)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L13 15 ANSWERS CAPLUS COPYRIGHT 2004 ACS on STN
CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
TI Synthesis and Characterization of a Highly Potent and Selective Isotopically Labeled Retinoic Acid **Receptor Ligand**, ALRT1550
ST ALRT1550 labeled analogs prepn **receptor** binding; retinoic acid **receptor** binding labeled ALRT1550
IT Retinoic acid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

IT 302-79-4, all-trans-Retinoic acid 71441-28-6, TTNPB
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

IT 178600-20-9P, ALRT1550 200556-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

IT 2359-09-3, 1,3-Benzenedicarboxylic acid, 5-(1,1-dimethylethyl)-
16225-26-6, 3,5-Di-tert-butylbenzoic acid 41891-54-7 50917-73-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

IT 22157-91-1P, 1,3-Benzenedimethanol, 5-(1,1-dimethylethyl)- 178688-27-2P
180740-53-8P, 1,3-Benzenedimethanol, 5-(1,1-dimethylethyl)-
α,α'-dimethyl- **180740-54-9P** 180740-55-0P
180740-56-1P 180740-57-2P 180740-58-3P 180740-59-4P 180740-60-7P
180740-61-8P 180740-62-9P 180740-63-0P 180740-64-1P 180740-69-6P,
1,3-Benzenedicarboxaldehyde, 5-(1,1-dimethylethyl)- 200556-34-9P
200556-36-1P 200556-38-3P 200556-39-4P 200556-41-8P 200556-61-2P
200556-63-4P 200556-64-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

IT 200556-27-0P 200556-44-1P 200556-45-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(isotopically labeled retinoic acid **receptor ligand**
ALRT1550)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
L1 STRUCTURE UPLOADED
L2 50 S SAM L1
L3 62637 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
L4 771 S L3 AND RECEPTOR
L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004
L8 10 S L4 AND MUSCARINIC
L9 68 S L5 NOT L6
L10 64 S L9 NOT L7
L11 61 S L10 NOT L8
L12 46 S L11 AND PY>1998
L13 15 S L11 NOT L12

=> d ibib abs l13

L13 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:447028 CAPLUS
DOCUMENT NUMBER: 129:221600
TITLE: Molecular Recognition on Functionalized Self-Assembled Monolayers of Alkanethiols on Gold
AUTHOR(S): Motesharei, Kianoush; Myles, David C.
CORPORATE SOURCE: Department of Chemistry Biochemistry, University of California, Los Angeles, CA, 90095-1569, USA
SOURCE: Journal of the American Chemical Society (1998), 120(29), 7328-7336
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A system for probing mol. recognition events at organic interfaces using fluorescent receptors is described. Receptors formed from the bis(2,6-diaminopyridine) amide of isophthalic acid are incorporated in mixed self-assembled monolayers (SAMs) of alkanethiols on gold and shown to interact with barbituric acid derivs. from solution Individual parameters that affect the ability of receptors on surfaces to recognize ligands from solution along with varieties of solvents for **ligand** solns. were examined
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs l13 2-15

L13 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:437199 CAPLUS
DOCUMENT NUMBER: 129:213752
TITLE: The use of affinity capillary electrophoresis for determining binding constants of ligands to receptors
AUTHOR(S): Zhao, Dong S.; Kwak, Eun-Soo; Kawaoka, Jane; Esquivel, Sally; Gomez, Frank A.
CORPORATE SOURCE: Univ. California, Riverside, CA, USA
SOURCE: American Laboratory (Shelton, Connecticut) (1998), 30(12), 40, 42-47
CODEN: ALBYBL; ISSN: 0044-7749
PUBLISHER: International Scientific Communications, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The paper reports on using affinity capillary electrophoresis (ACE) to determine binding consts. between three **receptor** -**ligand** combinations: carbonic anhydrase B and arylsulfonamides; vancomycin and the peptide N-acetyl-D-Ala-D-ALa; adamantane carboxylic acids and β-cyclodextrin derivs.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:307721 CAPLUS
DOCUMENT NUMBER: 129:41403
TITLE: A trivalent system from vancomycin·D-Ala-D-Ala with higher affinity than avidin·biotin
AUTHOR(S): Rao, Jianghong; Lahiri, Joydeep; Isaacs, Lyle; Weis, Robert M.; Whitesides, George M.
CORPORATE SOURCE: Dep. Chem. Chem. Biol., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Science (Washington, D. C.) (1998), 280(5364), 708-711

CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tris(vancomycin carboxamide) binds a trivalent **ligand** derived from D-Ala-D-Ala with very high affinity: dissociation constant (Kd) ≈ 4 + 10-17 ± 1 + 10-17 M. High-affinity trivalent binding and monovalent binding are fundamentally different. For example, in trivalent (and more generally, polyvalent) binding, dissociation occurs in stages, and its rate can be accelerated by monovalent **ligand** at sufficiently high concns. In monovalent binding, dissociation is determined solely by the rate constant for dissociation and cannot be accelerated by added monomer. Calorimetric measurements for the trivalent system indicate an approx. additive gain in enthalpy relative to the corresponding monomers. This system is one of the most stable organic **receptor-ligand** pairs involving small mols. that is known. It illustrates the practicality of designing very high-affinity systems based on polyvalency.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:48108 CAPLUS
DOCUMENT NUMBER: 128:75158
TITLE: Synthesis and Characterization of a Highly Potent and Selective Isotopically Labeled Retinoic Acid **Receptor Ligand**, ALRT1550
AUTHOR(S): Bennani, Youssef L.; Marron, Kristin S.; Mais, Dale E.; Flatten, Karen; Nadzan, Alex M.; Boehm, Marcus F.
CORPORATE SOURCE: Departments of Medicinal Chemistry and Endocrine Research, Ligand Pharmaceuticals Inc., San Diego, CA, 92121, USA
SOURCE: Journal of Organic Chemistry (1998), 63(3), 543-550
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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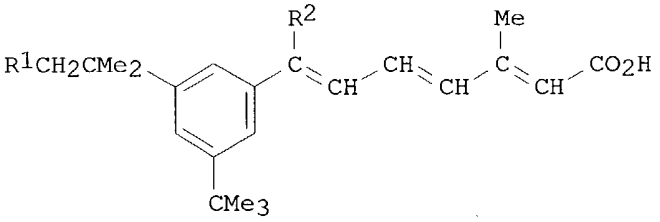

I

AB The syntheses of two labeled homologs of (2E,4E,6E)-7-(3,5-di-tert-butylphenyl)-3-methylocta-2,4,6-trienoic acid [ALRT1550, I (R1 = H, R2 = Me)], namely, [13CD3]ALRT1550 (I; R1 = H, R2 = 13CD3) and [3H]ALRT1550 (I; R1 = 3H, R2 = Me), are described. ALRT1550 is an exceptionally potent antiproliferative agent which is currently in phase I/II clin. trials for acute chemotherapy. Both homologs were prepared from com. available 3,5-di-tert-butylbenzoic acid. Homolog [13CD3]ALRT1550 was labeled at the 7-position of the trienoic acid chain via addition of [13CD3]MgI to a Weinreb amide precursor. The preparation of [3H]ALRT1550 utilized novel methodol. to prepare a sterically hindered and site-specific tritium-labeled tert-Bu group. Saturation binding and Scatchard anal. of this **ligand** at the

retinoic acid receptors are also described, along with competition binding (Ki) values for a series of known retinoids using [3H]ALRT1550 or [3H]ATRA as the labeled probes.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:719041 CAPLUS
DOCUMENT NUMBER: 126:74845
TITLE: Preparation of fluorescent **receptor** ligands
INVENTOR(S): McCabec, R. Tyler; Rhodes, Christopher A.; DeCosta, Bruce F.
PATENT ASSIGNEE(S): Pharmaceutical Discovery Corporation, USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 623,837,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5576436	A	19961119	US 1994-204559	19940302
PRIORITY APPLN. INFO.:			US 1991-739183	19910801
			US 1992-923837	19920731

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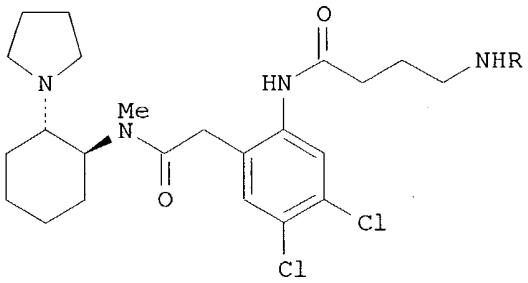

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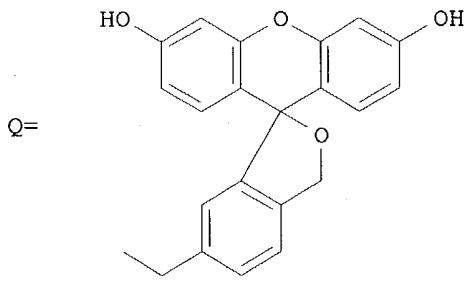


AB Title compds. comprise Conjugates of fluorescent labels with specific, selective, and high affinity ligands for receptors, e.g., NMDA, cannabinoid, glycine, etc. Thus, amine I (R = H) was amidated by fluorescein derivative R1R2 (R1 = fluorescein moiety Q, R2 = succinimidooxy) to give I (R = Q) as a κ1 opioid probe. Data for biol. activity of selected title compds. were given.

L13 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:681495 CAPLUS
DOCUMENT NUMBER: 126:26367
TITLE: Serotonin Dimers: Application of the Bivalent **Ligand** Approach to the Design of New Potent and Selective 5-HT1B/1D Agonists
AUTHOR(S): Halazy, Serge; Perez, Michel; Fourrier, Catherine; Pallard, Isabelle; Pauwels, Petrus J.; Palmier, Christiane; John, Gareth W.; Valentin, Jean-Pierre; Bonnafous, Regine; Martinez, Jean
CORPORATE SOURCE: Medicinal Chemistry Division, Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
SOURCE: Journal of Medicinal Chemistry (1996), 39(25), 4920-4927
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of serotonin dimers in which two serotonin moieties are linked together through their 5-hydroxyl residue has been prepared and evaluated as 5-HT1B/1D **receptor** agonists. Binding expts. at cloned human 5-HT1B, 5-HT1D, and 5-HT1A receptors show that all of these dimers are very potent ligands at 5-HT1B/1D receptors with increased binding selectivity vs. the 5-HT1A **receptor** when compared to serotonin. Studies of inhibition of the forskolin-stimulated c-AMP formation mediated by the human 5-HT1B **receptor** (formerly the 5-HT1Dβ **receptor**) demonstrate that all of these serotonin dimers behave as full agonists. Among them, the piperazide derivs. of bis-serotonin, 4g,j, were also identified as very potent agonists in contracting the New Zealand white rabbit saphenous vein (pD2 = 7.6 in each case compared to 5.8 for sumatriptan). Results anal. supports the hypothesis that the important increase in potency of the serotonin dimers can be attributed to the presence of two serotonin pharmacophores in the same mol., while the enhanced selectivity for 5-HT1B/1D **receptor** subtypes may be due to the position of the spacer attachment to serotonin.

L13 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:505199 CAPLUS
DOCUMENT NUMBER: 125:247557
TITLE: Halide anion recognition by new acyclic quaternary polybipyridinium and polypyridinium receptors
AUTHOR(S): Beer, Paul D.; Fletcher, Nicolas C.; Grieve, Alan; Wheller, John W.; Moore, Christopher P.; Wear, Trevor
CORPORATE SOURCE: Inorg. Chem. Lab., Univ. Oxford, Oxford, OX1 3QR, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1996), (8), 1545-1552
CODEN: JCPKBH; ISSN: 0300-9580
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New acyclic quaternary polybipyridinium receptors containing 5,5'- and 4,4'-disubstituted N,N'-dimethyl-2,2'-bipyridinium moieties and a polypyridinium **receptor** have been synthesized. 1H NMR titration studies in deuterated DMSO show that these receptors complex chloride and bromide anions, with a 1:1 stoichiometric **ligand**:chloride stability constant evaluations suggesting the amide containing polypyridinium **receptor** forms the most thermodn. stable chloride anion complex. Square-wave voltammetric investigations showed some of the polypyridinium receptors to recognize electrochem. the chloride anion.

L13 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:25017 CAPLUS

DOCUMENT NUMBER: 124:164460
TITLE: Antimetastatic activities of synthetic Arg-Gly-Asp-Ser (RGDS) and Arg-Leu-Asp-Ser (RLDS) peptide analogs and their inhibitory mechanisms
AUTHOR(S): Fujii, Hideki; Komazawa, Hiroyuki; Mori, Hideto; Kojima, Masayoshi; Itoh, Isamu; Murata, Jun; Azuma, Ichiro; Saiki, Ikuo
CORPORATE SOURCE: Res. Inst. Wakan-Yaku, Toyama Med. and Pharmaceutical Univ., Toyama, 930-01, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1995), 18(12), 1681-8
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have investigated the inhibitory effect of the N-terminal modified Arg-Gly-Asp-Ser (RGDS) analogs, AcDRGDS and AcDRLDS, on tumor cell adhesion to the components of extracellular matrix and basement membrane, and also tested the antimetastatic effect of their conjugates with trimesic acid, Ar(DRGDS)3 and AR(DRLDS)3. AcDRGDS significantly inhibited tumor cell adhesion to fibronectin, vitronectin and RGDS substrates, but not to CS1 substrate which is a **ligand** for the α4β1 tumor surfaces integrin **receptor**. In contrast, AcDRLDS variant peptide significantly inhibited tumor cell adhesion to laminin, in addition to RGDS-mediated adhesion to fibronectin and vitronectin. AcDRLDS also inhibited tumor cell adhesion to CS1 as well as the RGDS sequence within the fibronectin mol. in a concentration-dependent manner, although the inhibitory effect was less than that of the CS1 (EILDV) peptide. Ar(DRLDS)3 inhibited the laminin- and fibronectin-mediated invasion and migration of tumor cells, whereas Ar(DRGDS)3 inhibited the laminin- and fibronectin-mediated invasion and migration of tumor cells, whereas Ar(DRGDS)3 selectively inhibited exptl. lung or liver metastases of various types of murine and human tumors than the original RGDS-containing peptides or Ar(COONa)3. Multiple administrations of Ar(DRGDS)3 or Ar(DRLDS)3 potently inhibited spontaneous lung metastasis produced by intra-footpad injection of B16-BL6 cells without affecting the primary tumor size at the time of surgical excision, as compared with RGDS peptide or untreated control. Thus, AR(DRGDS)3 and AR(DRLDS)3 substantially increased the exhibiting any antimetastatic effect of the peptides without direct cytotoxicity.

L13 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:44283 CAPLUS
DOCUMENT NUMBER: 122:71336
TITLE: Non-peptide fibrinogen **receptor** antagonists. 4. Proposed three-dimensional requirements in centrally constrained inhibitors
AUTHOR(S): Naylor, A. M.; Egbertson, M. S.; Vassallo, L. M.; Birchenough, L. A.; Zhang, G. X.; Gould, R. J.; Hartman, G. D.
CORPORATE SOURCE: Dep. Biol. Chem., Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(15), 1841-6
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A three-dimensional description of **ligand** conformations consistent with GPIIbIIIa antagonist activity was developed from a systematic conformational search of centrally-constrained fibrinogen **receptor** antagonists.

L13 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:503388 CAPLUS
DOCUMENT NUMBER: 121:103388
TITLE: Molecular Recognition in Membrane Mimics: A Fluorescence Probe
AUTHOR(S): Motesharei, Kianoush; Myles, David C.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of California, Los Angeles, CA, 90024-1569, USA
SOURCE: Journal of the American Chemical Society (1994), 116(16), 7413-14
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

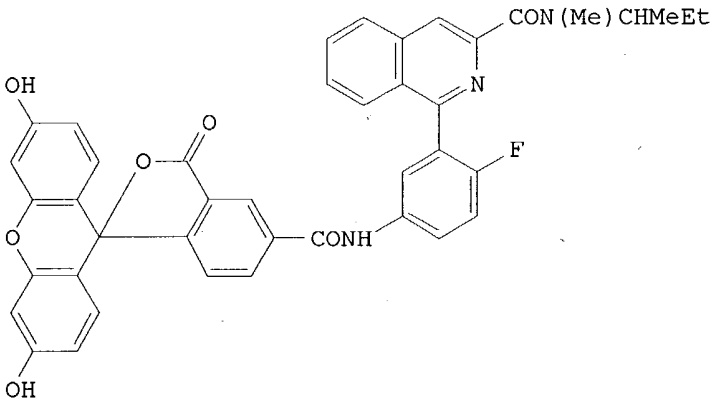
AB A system is described for probing mol. recognition events in synthetic membranes using the change in the wavelength of fluorescence of receptors upon binding of **ligand**. The bis(2,6-diaminopyridine) amide of isophthalic acid was used as the **receptor**. Mixed monolayer containing receptors functionalized with 10-carbon alkanethiol tethers and octanethiol were self-assembled on thin films of gold. A series of fluorescence expts. demonstrated that the presence of **ligand** by the **receptor**. The key evidence for interaction of the **ligand** and **receptor** was the reversible shift of the wavelength of fluorescence emission of the **receptor** in the presence and absence of the **ligand**.

L13 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:251070 CAPLUS
DOCUMENT NUMBER: 118:251070
TITLE: Characterization of specific drug receptors with fluorescent ligands, and fluorescent **ligand** preparation
INVENTOR(S): Mccabe, R. Tyler; Rhodes, Christopher A.
PATENT ASSIGNEE(S): Pharmaceutical Discovery Corp., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303382	A2	19930218	WO 1992-US6447	19920731
WO 9303382	A3	19930429		
W: AU, CA, HU, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9224071	A1	19930302	AU 1992-24071	19920731
US 5468854	A	19951121	US 1993-95937	19930722
PRIORITY APPLN. INFO.:			US 1991-739183	19910801
			WO 1992-US6447	19920731

AB Conjugates of fluorescent labels with specific, selective, and high-affinity **receptor** ligands are prepared The conjugates are used to directly measure binding to receptors (benzodiazepine receptors, opioid receptors, adrenergic receptors, K channels, etc.). The label portion of the conjugate may be fluorescein or derivative thereof, Texas red, coumarin, dansyl chloride, etc. Thus, κ1-opioid **receptor** fluorescent probe 1S,2S-trans-4,5-dichloro-2-(4-fluorescein-5-carboxamido)-n-butananido)-(N-methyl)-2-(1-pyrrolidinyl)-cyclohexyl)benzeneacetamide (preparation given) had an inhibitory constant vs. radioligand binding of 0.85 nM.

L13 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:584182 CAPLUS
DOCUMENT NUMBER: 117:184182
TITLE: AHN 683: a fluorescent **ligand** for peripheral-type benzodiazepine receptors
AUTHOR(S): McCabe, R. Tyler; Newman, Amy Hauck; Skolnick, Phil
CORPORATE SOURCE: Lab. Neurosci., Natl. Inst. Diabetes, Dig. Kidney Dis., Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1992), 262(2), 734-40
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB AHN 683 (I) is a fluorescein-derived **ligand** at peripheral-type benzodiazepine receptors structurally related to the isoquinoline carboxamide, PK 14105. The binding of AHN 683 to rat renal membranes measured by fluorescence techniques was saturable with a maximum number of binding sites of 2.3 ± 0.3 pmol/mg of protein. The KD (40.4 ± 2.2 nM) estimated by fluorescence was in good agreement with the Ki (77.4 ± 13.5 nM) obtained in competition studies with [3H] Ro 5-4864. AHN 683 exhibited rapid and reversible binding which was significantly reduced by the histidine modifying reagent, diethylpyrocarbonate. The potencies of a pair of isoquinoline carboxamide enantiomers as well as other structurally diverse peripheral-type benzodiazepine **receptor** ligands estimated by inhibition of AHN 683 binding were in good agreement with values obtained using radioligand binding techniques. AHN 683 binding was unaffected by compds. that do not recognize peripheral-type benzodiazepine receptors. Moreover, a significant increase in the maximum number of binding sites of AHN 683 to rat renal membranes after chronic furosemide treatment (29.2%, P < .02) was comparable to the increase measured using [3H]PK 11195 (35.6%, P < .001). These findings demonstrate the feasibility of using fluorescent **ligand** binding techniques to quant. characterize peripheral-type benzodiazepine receptors.

L13 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:207924 CAPLUS
DOCUMENT NUMBER: 116:207924
TITLE: MEP-surfaces as indicators for β2-adrenergic activity
AUTHOR(S): Koymans, Luc; Linschoten, Marcel R.; Wilting, Jaap; Janssen, Lamberg H. M.; Van Lenthe, Joop H.
CORPORATE SOURCE: Fac. Pharm., Utrecht Univ., Utrecht, 3584 CA, Neth.

SOURCE: Molecular Neuropharmacology (1991), 1(3), 149-54
CODEN: MOLNEO; ISSN: 0959-5244
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A possible relation between the 3D-mol. electrostatic potential (MEP) distribution around the aromatic nucleus of phenylethanolamines (both agonists and antagonist) and their intrinsic sympathomimetic activity (IA) is presented. MEPs are calculated at a distance of 1.5 Å from the van der Waals surface using the program package GAMESS at the ab initio LCAO-MO-SCF level invoking the STO3G minimal basis set. The most striking differences between agonists and antagonists occur in the region between the 4- and 5-position of the aromatic nucleus and to a lesser extent in the region around the 3- and 5-position. Agonists with a catechol-moiety form an intramol. hydrogen bond in which the substituent at the 3-position acts as hydrogen donor and the substituent at the 4-position as hydrogen acceptor. The inactivity of 6-halo substituted phenylethanolamine derivs. is most likely due to the induction of an unfavorable electrostatic field around the β-hydroxyl substituent rather than to conformational factors.

L13 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:94515 CAPLUS
DOCUMENT NUMBER: 114:94515
TITLE: Characterization of benzodiazepine receptors with fluorescent ligands
AUTHOR(S): McCabe, R. Tyler; De Costa, Brian R.; Miller, Rachel L.; Havunjian, R. Hratchia; Rice, Kenner C.; Skolnick, Phil
CORPORATE SOURCE: Lab. Neurosci., Natl. Inst. Diabetes, Bethesda, MD, 20892, USA
SOURCE: FASEB Journal (1990), 4(11), 2934-40
CODEN: FAJOEC; ISSN: 0892-6638
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Fluorescein conjugates of the high-affinity benzodiazepine **receptor** ligands Ro 15-1788 and Ro 7-1986 were synthesized. The binding of these fluorescent ligands [BD 621 (I) and BD 607 (II)] to benzodiazepine receptors was characterized by direct fluorescence measurement. Both the equilibrium dissociation consts. (KD) of BD 621 and BD 607 and the maximum number of binding sites (Bmax) estimated by fluorescence monitoring were consistent with values obtained by using radioligand binding techniques. The binding of BD 621 and BD 607 assessed by fluorescence measurement was reversible, abolished by photoaffinity labeling with Ro 15-4513, and unaffected by a variety of substances that do not bind to benzodiazepine receptors. The potencies of chemical diverse benzodiazepine **receptor** compds. to inhibit fluorescent **ligand** binding were highly correlated with potencies obtained from radioligand binding techniques. These findings demonstrate the feasibility of using direct fluorescence measurement techniques to quantitate **ligand**-**receptor** interactions.

L13 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:105485 CAPLUS

DOCUMENT NUMBER: 104:105485
TITLE: Mapping the turkey erythrocyte β- **receptor** : a distance geometry approach
AUTHOR(S): Linschoten, Marcel R.; Bultsma, Teake; Ijzerman, Ad P.; Timmerman, Hendrik
CORPORATE SOURCE: Dep. Pharmacochem., Free Univ., Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Medicinal Chemistry (1986), 29(2), 278-86
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Extensions and refinements of the **receptor** mapping method as originally developed by G. Crippen (1980) are presented. In a set of newly developed algorithms, measures are taken to reduce the number of required energy parameters to a statistically acceptable degree. The most important measure is the incorporation of lipophilicity as a hydrophobic bonding parameter to describe the binding of parts of the ligands to lipophilic areas on the **receptor**. To test the applicability of this set of programs, the turkey erythrocyte β **receptor** was mapped using a data set of J. P. Bilezikian et al. (1978). The exptl. determined free energies of binding can be reasonably described using a 9-point geometrical representation of the **receptor** site and only 6 energy parameters. The deduced model predicts that the Ph rings of phenylethanolamines and phenoxypropanolamines occupy different parts of the **receptor** site.

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 17, 2004 (20040917/UP).

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FILE 'REGISTRY' ENTERED AT 20:39:05 ON 23 SEP 2004
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L2 50 S SAM L1
L3 62637 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:48:04 ON 23 SEP 2004
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L5 73 S L4 AND LIGAND
L6 5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7 12 S L4 AND G (3W) PROTEIN

FILE 'STNGUIDE' ENTERED AT 21:01:25 ON 23 SEP 2004

FILE 'CAPLUS' ENTERED AT 21:02:16 ON 23 SEP 2004

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L8            10 S L4 AND MUSCARINIC
L9            68 S L5 NOT L6
L10           64 S L9 NOT L7
L11           61 S L10 NOT L8
L12           46 S L11 AND PY>1998
L13           15 S L11 NOT L12

     FILE 'STNGUIDE' ENTERED AT 21:14:07 ON 23 SEP 2004

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The indicated field code is not available for EXPAND in this
file.  To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

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FILE COVERS 1907 - 23 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004  (20040922/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


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E5             5     GRIFFIN J B/AU
E6             9     GRIFFIN J C/AU
E7            20     GRIFFIN J D/AU
E8             1     GRIFFIN J DENNIS/AU
E9            21     GRIFFIN J E/AU
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E11            1     GRIFFIN J E III/AU
E12           37     GRIFFIN J F/AU

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E3           24 --> GRIFFIN JOHN/AU
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E11           1      GRIFFIN JOHN FRANCIS THOMAS/AU
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L3         62637 S L1 FULL

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L6             5 S L5 AND (DIVALENT OR MULTIVALENT OR DIMERIC OR MULTIMERIC OR M
L7            12 S L4 AND G (3W) PROTEIN

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L11           61 S L10 NOT L8
L12           46 S L11 AND PY>1998
L13           15 S L11 NOT L12

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L15           24 S E3
L16           83 S L14 OR L15

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L3           62637 S L1 FULL

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L7              12 S L4 AND G (3W) PROTEIN

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                E GRIFFIN JOHN/AU
L15             24 S E3
L16             83 S L14 OR L15
L17              0 S L4 AND L16
L18              0 S L3 AND L16

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